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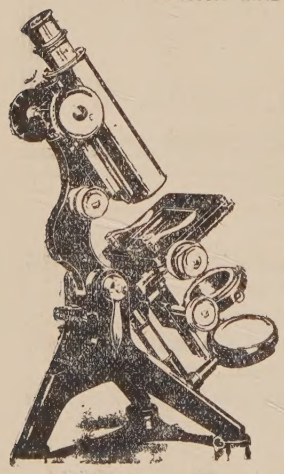

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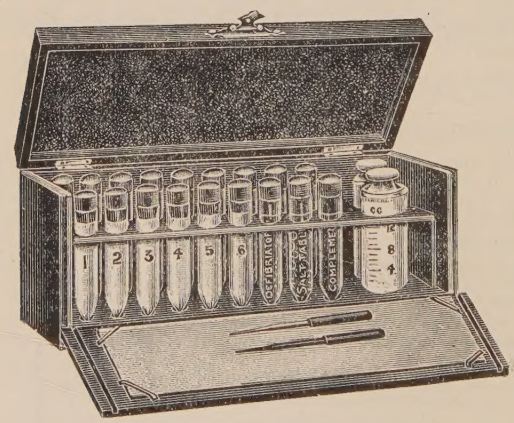

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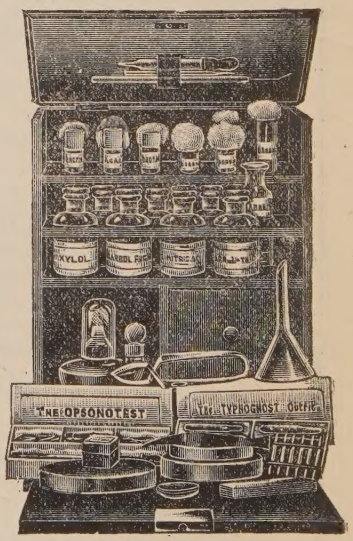

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TROPICAL DISEASES BUREAU.

TROPICAL DISEASES BULLETIN.

No. 1.] 1912. [Vol. I.

*KALA AZAR.

Indian Kala Azar.

Patton (W. S.). **The Development of the Parasite of Indian Kala Azar (*Herpetomonas Donovani*, Laveran and Mesnil) in *Cimex rotundatus*, Sign. and in *Cimex lectularius*, Linn. with some Observations on the Behaviour of the Parasite in *Conorrhinus rubrofasciatus*, de Geer.**—*Sci. Mems. by Officers of the Med. and Sanit. Depts. Govt. of India.* Calcutta. 1912. New Ser. No. 53. 38 pp. and 1 plate.

This is a fuller account of observations already briefly reported by the author (*Kala Azar Bulletin*, No. 3, p. 124). He first reviews his previous work, in which he showed that the leishmania failed to flagellate in *Pediculus capitis*, *Pediculus vestimenti*, *Culex fatigans*, *Neocellia stephensi*, *Stegomyia sugens* and *Ornithodorus savignyi*, but developed to the flagellate form in *Cimex rotundatus*. Since his earlier observations he has only on one occasion failed to find parasites in the peripheral blood in undoubted cases of kala azar and in this case they were found later by Donovan. He passes in review and criticises the experiments conducted by Basile, Sangiorgi, Alvares and Pereira da Silva, and Franchini.

Basile's flea transmission experiments are further criticised because of the difficulty of excluding natural infection in the dogs used and because he fails to mention the possible occurrence of piroplasma in these animals, though certain stages of this parasite in the spleen of dogs can readily be confused with leishmania.

In the experiments recorded in the present paper the author used only bugs which had been hatched in the laboratory, and had their first feed on a kala azar case in which parasites were numerous in the peripheral blood. Many of the bugs were fed several times and some had a feed from a second case of kala azar.

* Dr. Wenyon's review of the literature forms a continuation of the *Kala Azar Bulletin* (Nos. 1, 2, and 3, 1911-12).

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One batch however fed only once. As a result of the dissections it was found that the bugs which had fed shortly before for the second or third time were either uninfected or showed only the degenerating remains of flagellates which had developed from the parasites taken up at the first feed. In those bugs, however, in which a sufficient time had elapsed since the last feed on the case or which had had only a single feed, the developmental forms were much more numerous and in several an enormous multiplication had taken place and masses of rosettes were seen. This observation shows that for the complete development to take place it is essential that the bug does not have a second feed, for there is some substance in the blood of man which destroys the developmental forms. In two instances a similar destruction took place after the bugs had fed on a monkey, so this substance, which the author concludes is complement, occurs in the monkey also. To this fact he attributes the tendency of kala azar to remain endemic in Madras, and oriental sore in Cambay, without spreading beyond these limits, for the number of bugs capable of transmitting the disease must be greatly reduced by their habit of feeding repeatedly.

The point most emphasised by the author is that, after the ingested parasites have developed into the elongated flagellates, these again pass through a developmental process, terminating in the formation of small post-flagellate forms. These as a rule are slightly larger than the corresponding pre-flagellate forms; they resemble them only in shape, for they show marked differences in staining reaction. The formation of these post-flagellate forms from the flagellate commences on about the eighth day and is completed by the twelfth. The mature flagellates on the seventh to the ninth days become altered in appearance, the blue-staining protoplasm characteristic of the earlier forms gives place to a pink-staining protoplasm, and these forms gradually give rise to the post-flagellate forms. The author points out that it is important to note that when they appeared in the bugs the post-flagellate forms were the predominating forms, whereas in the bugs dissected a few days previously flagellates predominated.

The author believes that the post-flagellate forms gain entrance to a new host by being regurgitated from the gut while the bug feeds, for the whole of this development takes place in the mid gut. The development takes place in *Cimex lectularius* as well as in *Cimex rotundatus*; so that the author believes that the parasite of Mediterranean kala azar will be found to undergo its development in *Cimex lectularius*. He finds himself in complete agreement with Gabbi, who does not think that the cases of Mediterranean kala azar are of canine origin.

The author then criticises the view that has been put forward by some observers (Mesnil, Wenyon) that the development of leishmania in the bug takes place on account of the large quantity of blood in the stomach and is comparable to the culture in the test tube. Against this view it is pointed out that, though the blood suckers mentioned at the commencement of this review all suck up quantities of blood, there is no development of the parasite in them. The same lack of development was noted in the

case of the nymph of *Conorrhinus rubrofasciatus*, though this is about as large as the adult Cimex and gorges itself with blood. He doubts very much whether the forms seen by Wenyon in *Stegomyia fasciata* which had fed on oriental sores in Bagdad were in reality developmental forms of leishmania.

The author then discusses the biological position of the parasite of kala azar. He points out that it agrees with the typical Herpetomonas of an insect in having a pre-flagellate, a flagellate and a post-flagellate stage, so that he sees no reason for placing it in a new genus. He writes:—

"As the parasite of sleeping sickness passes one stage of its life history in the blood and organs of man and its multiplicative stage in an invertebrate, *Glossina palpalis*, so in the same way the parasite of Indian kala azar passes one stage of the life history in the blood and organs of man and its multiplicative stage in an invertebrate, *Cimex rotundatus*; there would, however, be no justification for placing the parasite of sleeping sickness in any other genus but the Trypanosoma."

[It is however this agreement with the life history of the trypanosome that justifies the genus *Leishmania*. For *Trypanosoma gambiense* agrees with other species of trypanosome in having a vertebrate and an invertebrate host, whereas the parasite of kala azar differs from the true Herpetomonas in having two hosts, the true Herpetomonas having only one and that an invertebrate. The fact that the parasite of kala azar has two, a vertebrate and invertebrate host, distinguishes it at once from the Herpetomonas.]

In a note to the paper Captain Patton records the successful intraperitoneal inoculation of a white rat with the parasite of Indian kala azar. The rat was inoculated with 3 cc. of emulsion of spleen from a case of kala azar. Fifteen days later it received a second injection of 1 cc.; it died two hours later. Its liver and spleen were considerably hypertrophied and contained large numbers of typical parasites. This is the first instance in which an animal has been infected with Indian kala azar.*

C. M. Wenyon.

Sudan Kala Azar.

Marshall (W. E.). **Further Experimental Investigation into Sudan Kala Azar.**—*Jl. R. Army Med. Corps.* 1912. Sept. Vol. 19. No. 3. pp. 276–280. With 1 plate.

In previous publications it was shown that the Sudan kala azar affects people of all ages, but is most common in late childhood or early adult life; that the grey monkey (*Cercopithecus sabaeus*) can be infected by intraperitoneal or subcutaneous injection of virus; that the parasite grows readily in ten per cent. citrate on Novy and Macneal's medium and in Nicolle's medium; and that the parasite is present in the peripheral blood in a large percentage of the cases. The author now points out that,

* Dr. Row has reported, in a paper shortly to be published, the successful inoculation of monkeys subcutaneously on the forehead with *Leishmania donovani*. In one case the virus was obtained from the spleen of a case of kala azar; in the other, cultures were used. Two monkeys developed at the site of inoculation lesions which contained leishmania and resembled oriental sore.

whereas it was formerly stated that the parasites were not numerous when present in the peripheral blood, two cases have since been examined in which they were very numerous; one patient was in an early stage of the disease and the other in an advanced stage. The eosinophile cells are usually much diminished or absent from the peripheral blood; this feature is of some help in differentiating kala azar from malaria. No drug has been of any use in checking the course of the disease. It has been found that dogs, especially young ones, are susceptible to the Sudan kala azar and that, though they can be infected by injecting emulsions of the organs of other infected dogs or monkeys, the injection of material obtained by spleen puncture from man is most certain. Of four dogs injected one was killed on the 145th day; the others died on the 128th, 95th and 74th days respectively.

Attempts were made to transmit the disease from one dog to another by keeping a healthy and infected dog in the same room and introducing dog fleas. The dogs were in contact for thirty-seven days, but no infection occurred. In another experiment a pup was put in a box with a dog for 124 days four days after the latter was inoculated. The dog became infected, but the pup was free from infection when killed two months later. A similar experiment was carried out with ticks, but was also unsuccessful. A series of experiments was carried out to determine by what means the disease may be conveyed from monkey to monkey. In each case a healthy and infected monkey were kept together in a cage. In some cases the monkeys were freed from all insects; in others they were not. In some the cages were of close gauge; in others they were open, so that mosquitoes could enter. In no case did a certain infection take place. The author points out that though it is generally possible to infect monkeys one of these animals was naturally immune.

C. M. W.

Mediterranean Kala Azar.

Lignos (Antoine). **Absence des Leishmania à l'Autopsie d'un Enfant mort de Kala Azar.**—*Bull. Soc. Path. Exot.* 1912. June. Vol. 5. No. 6. pp. 349–351.

A case of kala azar in a female child of 23 months came under observation in the Isle of Hydra in October 1911. The author performed spleen puncture on March 6th, 1912, and discovered numerous leishmania in the smears. On April 12 the child was treated by some aged women in such a manner that it died suddenly from dyspnoea. An autopsy was performed eighteen hours after death and though the body was in good condition no leishmania could be discovered in the smears. The author contents himself with recording the fact, and offers no explanation of the complete disappearance of the parasites in a period of one month intervening between the date of spleen puncture and the child's death.

C. M. W.

CARDAMATIS (Jean P.). **Le Kala Azar est en Grèce une Maladie à Cas sporadiques.—Mégalosplénies de Cause inconnue.**—*Bull. Soc. Path. Exot.* 1912. July. Vol. 5. No. 7. pp. 489–491.

The author requested the medical practitioners in various parts of Greece to send him films of material obtained from the puncture of spleens in cases of suspected kala azar. In an examination of these films, and of three others from cases which came under the author's notice, leishmania were found in two cases only, from the province of Patras. The author points out that, outside the endemic centres in the islands of Spezzia and Hydra and the district around Patras and probably also the islands of Cephalonia, Ithaca and Paxos, kala azar is not as common as was at first thought. In the rest of Greece the cases occur sporadically; they have been reported in isolated instances from Athens, Piraeus, Nauplia, Almyros, Volo, Trikkala, Poros and elsewhere. Between May 1910 and the date of this paper fifty cases have been notified in Greece. The author points out that leishmania have never been found in the peripheral blood of these cases of kala azar and that a disease other than leishmaniasis, characterised by splenomegaly, exists in Greece.

C. M. W.

JEMMA (R.). **Considerazioni sopra Sessantatrè Casi di Anemia da Leishmania osservati nella Clinica Pediatrica di Palermo.** [On sixty-three Cases of Kala-Azar seen at Palermo.]—*Riforma Medica.* 1912. Aug. 24. Vol. 28. No. 34. pp. 925–930.

These cases were seen at the clinic at Palermo between October 1909 and August 1912. The majority came from the suburbs and outlying districts, only three from Palermo itself. The cases occur, as a rule, quite sporadically, but certain endemic centres exist. The association of the disease with that of dogs forms the subject of a separate paper, *vide* p. 11. The author believes that the disease is transmitted from dogs to children, as was first suggested by NICOLLE and demonstrated by BASILE. Of the 63 patients five were over four years of age, the eldest being six; 35 were males and 28 females; most were from families in poor circumstances. The chief symptoms of the disease are considered, but nothing new is recorded. The parasite has been cultivated on the NNN medium, on a similar medium made up with human serum and ascitic fluid, and on the Bordet and Gengou medium.

As regards prognosis, of the 63 cases twelve were lost to view after the first visit, 38 have died, five are in a serious condition, four are stationary, one is much improved, and three have recovered. These three patients have been in perfect health for over a year and search for the parasite has been unsuccesssful, though in two the spleen has not yet quite regained its normal volume. In earlier publications the author stated that he doubted if spontaneous recovery ever occurred. He now modifies this view and agrees with NICOLLE, SPAGNOLIO and LIGNOS, who have recorded recoveries. There was no possibility of an error of diagnosis in the three cases, for parasites had been discovered in each. None of the therapeutic measures

adopted was of any avail; the recovery of the three patients was not due to any special line of treatment. It is pointed out that after the common diseases—tuberculosis, the exanthemata, and diphtheria—the most frequently encountered infectious malady in Palermo is infantile kala azar; the author believes it to be widely spread in this district.

C. M. W.

CARYOPHYLLIS (G.) and SOTIRIADES (D.). **Zur Behandlung und Heilung des Kala-Azar mit Salvarsan.** [The Treatment and Cure of Kala Azar by Salvarsan.]—*Deut. Med. Wochenschr.* 1912. Aug. 15. Vol. 38. No. 33. p. 1554.

The authors refer to their earlier paper on this subject (see *Kala Azar Bulletin* No. 2, p. 92). The present one records the treatment of a case of infantile kala azar in Greece. The child was under treatment for seven months and in this time received intravenous injections of salvarsan every eight or fifteen days in doses of 0·3-0·4 grams, in all three grams. Since the treatment was suspended all signs of the disease have vanished. The authors regard their patient as having been cured by the drug. They point out that to give a drug by the intravenous method is a difficult operation in a small child, so that the general failure of salvarsan in this disease is due to the employment of the more easily applied intramuscular method. That the recovery of the case was due to the treatment and not to nature is shown by the fact that each injection was followed by signs of improvement.

C. M. W.

Di CRISTINA (G.). **Ancora sulla Deviazione del Complemento nella Anemia da Leishmania.** [On Complement Deviation in Infantile Kala Azar.]—*Pathologica.* 1912. July 15. Vol. 4. No. 89. pp. 409–410.

The author is led to publish his results, though only seven cases have been studied, on account of the paper of MAKKAS and PAPASSOTIRION (reviewed in *Kala Azar Bulletin* No. 2, p. 88). These authors claim that the deviation of the complement is of constant occurrence in infantile kala azar and is thus of diagnostic importance. Di Cristina has not been able in his cases to demonstrate the presence of any antibody in the blood in spite of the most careful observations and precautions in the preparation of the antigen, which moreover gave positive results in the case of rabbits injected with cultures of leishmania. The technique was that generally used in the Wasserman reaction. The spleen of a child which had died of kala azar was used. It contained an enormous number of parasites. The organ was broken up and dried in vacuo. Tests were made also with cultures of the parasites killed by an hour's exposure to a temperature of 55° C. The author points out that Professor LONGO has obtained similar negative results, so that the reaction cannot be of diagnostic importance, as MAKKAS and PAPASSOTIRION maintain. He believes however that the absence of a reaction indicates that the organism does not react to the infection.

C. M. W.

Di Cristina (G.) and Caronia (G.). (i.) **Primi tentativi di Vaccinazione graduale nell' Anemia da Leishmania con Culture morte.** [Attempts to treat Infantile Kala Azar by Vaccination with Killed Cultures of Leishmania.] (ii.) **Sulla Presenza di Ambocettori specifici in Bambini affetti da Anemia da Leishmania guariti Spontaneamente.** [On Specific Amboceptors in the Blood in Cases of Infantile Kala Azar which have recovered Spontaneously.]—*Pathologica.* 1912. Sept. 1. Vol. 4. No. 92. pp. 519–522 and pp. 534–535.

(i.) Caronia has shown that the injection of killed cultures into healthy children causes the formation of antibodies and Di Cristina has shown the same in the case of rabbits. The following technique was used. A culture of the leishmania was obtained by spleen puncture of the child to be treated. The NNN medium was used and the culture allowed to develop for ten days, after which the water of condensation contained a fairly uniform number of flagellates. The cultures were inactivated at a temperature of 55° C. Ten cubic centimetres of culture were injected in ten days. After the tenth injection blood was taken from the finger and tested for the reaction of complement deviation, an aqueous extract of a dried, heavily infected, kala azar spleen being used as antigen. Seven cases were treated in this way. The authors found that the course of the disease was in no way altered. About a month after the treatment two of the cases had died. In one case the treatment produced a marked leucocytosis, while in the others there was only a slight increase in the leucocytes. An important result was the appearance in every case of a specific amboceptor though before treatment there was no specific antibody in the blood, a result showing that the organism under the stimulus of dead cultures is able to acquire an immunity reaction. It is pointed out that a similar absence of spontaneously produced immunity reaction is seen in the case of suckled infants suffering from syphilis or tuberculosis, and that in the latter disease injection of tuberculin will assist in the development of specific antibodies.

(ii.) In the second paper the authors record two instances of spontaneous recovery from kala azar. In both cases parasites had been demonstrated by spleen puncture. In both the recovery was accompanied by disappearance of the febrile symptoms, reduction in the size of the spleen, and an amelioration of the general condition. The authors found that the recovery in both cases was associated with the presence of a specific amboceptor in the blood. The test was conducted as in the other cases with the aqueous extract of the heavily infected spleen as antigen. This observation supports their hypothesis that the severity of the disease is due to the absence of immunity reaction, and justifies their attempt to produce such an immunity by the injection of killed cultures. The paper closes with an account of the clinical features of the two cases.

C. M. W.

CANNATA (Sebastiano). **Sul Potere Agglutinante del Siero di Sangue nell'Anemia da Leishmania rispetto ad alcuni Germi Patogeni.** [The Agglutinating Power of Blood Serum of Cases of Infantile Kala Azar with reference to other Pathogenic Organisms.]—*Pathologica.* 1912. Aug. 15. Vol. 4. No. 91. p. 482.

The author has tested the agglutinating power of the serum of twenty cases of infantile kala azar against the following organisms—*Micrococcus melitensis, Bacillus typhosus, B paratyphosus* A and B, and the bacillus of Koch. None of the cases gave any agglutination of the last-named organism. Four serums agglutinated the *melitensis,* three in dilutions of 1:25 and one in a dilution of 1:10. One of the first three agglutinated in addition the three organisms of the typhoid group in dilutions of 1:10, and another of these agglutinated the paratyphoid B in a dilution of 1:25. The cases giving agglutination were in children varying in age from thirteen to 24 months and the disease was of twenty days to ten months' duration. The author does not state whether he has made control tests with healthy children.

C. M. W.

PETROW (N. W.). **Ein Fall von Kala-Azar.** [A Case of Kala-Azar.]—*Virchow's Archiv f. Path. Anat. u. Physiol.* 1912. Sept. 7. Vol. 209. No. 3. pp. 453–456. **Sluchai tropicheskoi Splenomegali** (Kala Azar).—*Russk. Vrach.* 1912. No. 26.

In these papers the author gives a detailed account of the disease and post mortem findings in a case of kala azar in a woman 38 years of age, who died of that disease after returning to St. Petersburg from Tschardschui in Turkestan. The symptoms noted do not call for particular mention, but it is interesting as being the first recorded case of the disease in an adult from that district, other cases having been in young children.

C. M. W.

SPAGNOLIO (G.). **Sulla Vitalità della *Leishmania donovani* in simbiosi con i Germi delle Malattie Infettive Intestinali e con lo Streptococco piogene.** [On the Vitality of *L. donovani* in Symbiosis with Bacilli of Various Intestinal Infections and with *Streptococcus pyogenes.*]—*Malaria e Malat. d. Paesi Caldi.* 1912. May–June. Vol. 3. No. 5/6. pp. 151–152.

This paper describes experiments made to test the effect of various organisms (*Bacillus coli,* Gärtner's bacillus, Shiga's bacillus, Flexner's bacillus, *Bacillus typhosus, B. paratyphosus* A and B, *Micrococcus melitensis* and the comma bacillus of Koch) on cultural forms of leishmania. The experiments were conducted in three ways: firstly by adding flagellate forms of leishmania to well developed cultures of the organisms, secondly by inoculating a fully developed culture of leishmania with the organisms, and thirdly by inoculating the medium simultaneously with

the leishmania and the bacilli. All these organisms except the *Micrococcus melitensis* proved fatal to the flagellates, which disappeared from the cultures as the bacteria multiplied. Even in the second series, in which the bacteria were added to a well developed culture of flagellates, these survived only 24 to 36 hours. Similar results were obtained with streptococci and staphylococci. In the case of the *M. melitensis* added to well developed culture of leishmania the flagellates were still alive after fourteen or fifteen days, after which time they gradually disappeared as the bacteria developed. *M. melitensis* is thus seen to be the only organism with which the leishmania will grow for any length of time.

C. M. W.

FRANCHINI (G.). **Leishmanie e Zanzare.** [Leishmania and Mosquitoes].—*Riforma Medica.* 1912. Sept. 7. Vol. 28. No. 36. pp. 981–982.

In his earlier papers the author has shown that mosquitoes can be infected with the leishmania of infantile kala azar by feeding them on cultures of the organism. He has now fed mosquitoes, obtained from the plains round Catania, on material obtained by spleen puncture, and has thus induced them, though with the greatest difficulty, to take up unaltered parasites. These were found in the mosquitoes after four, six, and eight hours, some in unaltered condition, others slightly changed. Some appeared to be degenerating; others were in groups of five to six, or eighteen to twenty parasites. No flagellate forms were seen. After thirty hours some large forms were detected, comparable with the large non-flagellate forms met with in cultures. After 48 hours in two preparations many parasites were found, some in rosettes, some in masses composed of numerous parasites closely resembling leishmania. Still no flagellate forms were seen. Finally, in one preparation from a mosquito which had taken up spleen juice four days before flagellates were found, and the author had no hesitation in identifying these with leishmania. He states that he has avoided the possibility of confusing these forms with natural flagellates of the mosquito by dissection of many control mosquitoes, in which no flagellates having the remotest resemblance to the leishmania could be found.

C. M. W.

VISENTINI (Arrigo). **Mécanisme de l'Immunité Naturelle du Rat et du Cobaye à l'égard des Cultures de *Leishmania infantum*.**—*Bull. Soc. Path. Exot.* 1912. June. Vol. 5. No. 6. pp. 358–360.

The author has attempted to infect twenty guinea-pigs and ten rats by the intraperitoneal injection of 2-4 cc. of culture of *Leishmania infantum.* The animals were examined from two hours to 93 days after inoculation, but in no case was any flagellate found, nor did culture from the peritoneal fluid yield a positive result. The guinea-pig and white rat possess a natural immunity against *Leishmania infantum.* The author recalls the fact that FRANCHINI recorded the infection of a guinea-pig by intraperitoneal injection of culture (see *Kala Azar Bulletin*, No. 1, p. 8). The author examined the nature of the immunity of his guinea-pigs; he found that within five minutes after injection into the peritoneal

cavity the flagellates are adherent to the leucocytes and soon become ingested by them. Within the leucocytes they quickly degenerate till only the nuclei remain. After three hours no vestige of the organisms can be found. During this time the flagellates never leave the peritoneal cavity as they cannot be found in the circulation. Culture of the flagellates has been obtained up to one and a quarter hours after injection into the peritoneal cavity.

[VISENTINI's experiments resemble those of DELANOË on the natural immunity of mice. (*Kala Azar Bulletin* No. 1, p. 53.)]

C. M. W.

YAKIMOFF (W. L.) et KOHL-YAKIMOFF (Nina). **L'Infection des Animaux de Laboratoire par la *Leishmania infantum* Ch. Nicolle. (Deuxième note preliminaire).**—*Bull. Soc. Path. Exot.* 1912. June. Vol. 5. No. 6. pp. 355–357.

In a former note (see *Kala Azar Bulletin* No. 3, p. 140) the authors showed that it was possible to produce a general infection in mice by intravenous injections of cultures of *Leishmania infantum*. They now record the production of a general infection in two dogs by such injections, and the infection of mice and rats by the inoculation of material from the organs of the dogs. Material obtained from the organs of these mice produced infection in other mice and also in one rat. In the former paper it was stated that the organs of mice infected by cultures had been injected into other mice. It is here stated that these mice became infected. The authors point out that the experiments, which are still in progress, demonstrate the possibility of carrying on a strain of leishmania in mice. It is important to note that in several instances in the case of rats and mice where microscopic examination had been negative as regards the presence of leishmania the culture test gave a positive result.

C. M. W.

MANTOVANI (Mario). **Infezione sperimentale da *Leishmania donovani* nel Coniglio. (Nota preventiva.)** [Experimental Infection of Rabbit with *L. donovani*.]—*Pathologica.* 1912. July 15. Vol. 4. No. 89. p. 415.

The author records the successful inoculation of a rabbit by the injection of one cubic centimetre of culture of leishmania into the marginal vein of the ear. Twenty days later the rabbit, which had become very thin, was killed. Both by culture and by examination of smears from the organs it was shown to have a general infection with leishmania.

C. M. W.

CANINE KALA AZAR.

NICOLLE (Charles) and CONOR (M.). **Quelques Expériences pratiquées avec le Virus de la Leishmaniose naturelle du Chien. Reproduction de la Maladie chez le Singe.**—*Bull. Soc. Path. Exot.* 1912. June. Vol. 5. No. 6. pp. 351–355.

The authors point out that kala azar has been successfully transmitted from one dog to another by inoculation in only one instance (SENEVET—*Kala Azar Bulletin* No. 3, p. 139). The present paper records the successful inoculation of two dogs from

the organs of a dog which had been found naturally infected at Tunis. A further passage was made by inoculating the organs of one of these dogs into three other dogs and two monkeys. Of the three dogs only one became infected and its organs failed to infect another dog. One of the two monkeys (*Macacus sinicus*), a young one, became infected; its organs failed to infect a dog and a monkey. It is interesting to note that its death was due to sudden dyspnoea, a common cause of death in children suffering from the disease. Cultures were obtained from the first subinoculated dog. Their agreement with cultures of leishmania obtained from cases in children is absolute. The injection of fifty cultures intraperitoneally in two doses with an interval of 24 hours failed to infect a monkey, which died 49 days later. It is pointed out that young dogs are more readily infected than older ones.

C. M. W.

JEMMA (ROCCO). **Sulla Leishmaniosi del Cane nei Dintorni di Palermo.** [Leishmaniasis of Dogs in the Environs of Palermo.] —*Pathologica.* 1912. Aug. 1. Vol. 4. No. 90. pp. 466–467.

The author points out that a previous examination of 227 dogs of Palermo for evidences of leishmania infection was negative (*Kala Azar Bulletin* No. 1, p. 17). In the investigation here recorded Dr. Carlo BASILE collaborated. Two cases of infantile kala azar, one from Carini and the other from S. Maria di Gesù, villages in the vicinity of Palermo, were studied as to their possible association with the disease in dogs. In the case of the child from Carini it was found that a dog in a neighbouring house was heavily infected with leishmania and the parents of the child admitted having killed their own dog on account of its bad condition. In the case of the second child such a direct association was not ascertained, but a masterless dog in poor condition was found to be harbouring leishmania. It has thus been demonstrated that canine kala azar occurs in all the endemic centres of the infantile disease on the Mediterranean littoral, Palermo hitherto having been regarded as an exception to this rule.

C. M. W.

TROPICAL SORE.

SPLENDORE (A.). **Leishmaniosi con Localizzazione nelle Cavità Mucose (Nuova Forma Clinica).** [Leishmaniasis with Lesions of the Mucous Cavities (a New Clinical Form).]—*Bull. Soc. Path. Exot.* 1912. June. Vol. 5. No. 6. pp. 411–438. With 1 plate.

In this memoir the author describes in detail his observations upon three cases of the Brazilian leishmaniasis, which is peculiar in that it produces lesions not only of the skin on the exposed parts of the body, but also of the mucous membranes of the nose, mouth, pharynx and larynx. Its features were well described in an earlier paper by the author and also by CARINI (*Kala Azar Bulletin* No. 2, pp. 104-105), and later by ESCOMEL under the name of La Espundia and by LAVERAN and NATTAN-LARRIER (*Kala Azar Bulletin* No. 3, pp. 167 and 168).

The author points out that the lesions on the skin resemble closely those of oriental sore, whereas the nasal, buccal, and pharyngeal lesions take the form of vegetations of framboesial type. An important feature of the disease, emphasised by the

author, is the occurrence of irregular fever in periods of several days duration. It is usually attributed to malaria, but is resistant to quinine, and other evidences of a malarial affection are wanting. The lymphatic glands in the neck are enlarged and have been shown to contain leishmania. The blood shows a leucocytosis (12-16 thousand) with an increase in the large mononuclears. Leishmania have not been found in the peripheral blood except in that taken from the neighbourhood of the lesions. As regards treatment, nothing reduces the lesions in the mouth and nose; the author has tried radium exposures, X-rays, and injections of 606. Radium exposures are however, very efficacious in the case of the cutaneous lesions, which are quickly healed.

The leishmania which have been found by the author in the various lesions differ in no way from those of oriental sore. In pharyngeal growths, however, there occur some curious elongated forms, some of which are provided with flagella and thus resemble the forms seen in artificial culture. The parasites have been cultivated in the usual way on NNN medium; the cultures did not differ from those of oriental sore obtained by NICOLLE. Experimentally the author has been successful in inoculating the virus from man into two monkeys (*Mico estrella*); with other animals he was unsuccessful. The injection of cultures in large quantity both intraperitoneally and subcutaneously into various animals (dog, rabbit, guinea-pig, rat, bat, cat, pigeon, bird, frog) was without result except in the case of one rat killed after a month which showed peculiar red granules in the spleen and liver like nuclei of leishmania. A monkey (*M. estrella*) inoculated in the frontal region with culture developed a small papule after forty days; no leishmania were found and it disappeared in fifteen days.

The author has not been able to solve the problem of transmission.

C. M. W.

WENYON (C. M.). **A Supposed Peculiarity in the Structure of the Leishmania from Skin Lesions in South America.**—*Jl. Trop. Med. & Hyg.* 1912. July 1. Vol. 15. No. 13. pp. 193–194.

The author calls attention to the paper by LAVERAN and NATTAN-LARRIER (*Bull. Soc. Path. Exot.*, 1912, p. 176), describing a peculiarity in the leishmania from South America which they regard as of constant occurrence. It is stated by them that the trophonucleus instead of being round is very much flattened out, and lies like a rod or band along one side of the capsule of the parasite. The author points out that parasites showing this peculiarity are to be found in films of the Bagdad sore, and that in smears from South American sores many of the leishmania show the typical structure with a rounded trophonucleus, so that the flattening of the trophonucleus cannot be held to be a feature peculiar to the South American leishmania.

[In a more recent paper, reviewed below, LAVERAN and NATTAN-LARRIER record the finding of typical leishmania in cases of Espundia from South America.]

C. M. W.

LAVERAN (A.) and NATTAN-LARRIER. **Contribution à l'Étude de la Espundia. (Deuxième Note.)**—*Bull. Soc. Path. Exot.* 1912. July. Vol. 5. No. 7. pp. 486–489.

The following history of a case of Espundia is given.—A man 62 years of age had been 55 days in the mountainous region of Peru where Espundia occurs. He was bitten on the margin of the ear by some black fly. Fifteen days later an ulcer appeared at this spot and after one year the disease had so extended that in addition to the initial lesion on the ear there were ulcers on the feet, fingers, nose, mucosa of the nasal fossa, palate, pharynx, and larynx. The development of the disease was thus very rapid. In smears from the ear, nose, and throat lesions leishmania were discovered. Many of these had the structure of the classical leishmania, while others had the flattened nucleus, which the authors have called attention to in a previous paper. Reference is made to the work of SPLENDORE on the leishmaniasis of Brazil (*v. supra*). It is suggested that, just as one distinguishes *Leishmania donovani* and *Leishmania tropica* as two species, so it will be convenient to regard the American form as a variety under the name of *L. tropica* var. *americana.*

C. M. W.

SEIDELIN (Harald). **Leishmaniasis and Babesiasis in Yucatan.**—*Ann. Trop. Med. & Parasit.* 1912. July 31. Vol. 6. No. 2. pp. 295–299.

During a recent expedition to the Southern Mexican States the author examined six cases of a disease which is said to be widely distributed through the Yucatan peninsula. It commences as a rule in the form of an eroding ulcer on the margin of the ear. In one of the cases there was in addition a non-ulcerating nodule on the cheek; in others there were sores on the arm and leg. Leishmania were found in four cases and in largest number from the non-ulcerating nodule on the cheek. The author has noted the association of the leishmania with a diplococcus resembling the gonococcus. This was present in the cheek nodule. The author is "inclined to regard this coccus as primarily associated with the leishmania, in which case it would probably be of pathogenic importance."

[These cases are evidently of the same nature as those described by DARLING and CONNOR from Panama. (*Kala Azar Bulletin* No. 2, p. 110.)]

C. M. W.

WENYON (C. M.). **A Case of Dermal Leishmaniasis from S. America, with some Remarks on the Structure of the Parasite and its Culture.**—*Jl. London School of Trop. Med.* 1912. July. Vol. 1. No. 3. pp. 207–211. With 1 plate.

In this paper is described the case of an Englishman who contracted the disease on a journey through Peru and Bolivia. He had a raised granulomatous tumour, about three centimetres in diameter, over the right eye and nose, and a small depressed ulcer at the outer corner of the right eye. There was much

oedema of the eyelid on that side and the glands under the jaw were enlarged. Two hard lymphatic cords crossed the face from the neighbourhood of the sores to the enlarged glands. Leishmania were discovered in both the sores and from them a culture of the organism was obtained on NNN medium. The cultures closely resembled those of other types of leishmania. The parasites from the sore itself did not differ in any way from those obtained from the oriental sores of Bagdad and elsewhere. In the present case there were no lesions on the mucosa of the nose or mouth; the condition thus resembled the early stage of the disease described by Escomel, and Laveran and Nattan-Larrier (*Kala Azar Bulletin* No. 3, pp. 167 and 168) and by Splendore in the paper reviewed above. The case was treated in two ways. Injections of killed cultures of the leishmania were first given, but these had apparently little, if any, effect. Accordingly the ointment recommended by Cardamatis and Melissidis, consisting of equal parts of methylene blue, lanoline, and vaseline, was used twice a day. Under this treatment the small sore healed completely in about one month and at the date of the paper the large sore had considerably improved. [It may be of interest to mention here that the large sore was treated with the ointment for two and a half months, and as it then showed some sign of healing the applications of methylene blue ointment were stopped. The sore had completely healed in another two weeks. Over three weeks have now elapsed and there is no sign of any recurrence. The glandular enlargement has almost completely disappeared.]

With material obtained from the sore a monkey (*Cynocephalus*) and a dog were inoculated on the ears and nose. After four months the monkey developed a papule on each ear and one on the nose. In the ear papules leishmania were found. The dog developed nodules on each ear after three months, but not on the nose. Leishmania were found in these lesions also.

C. M. W.

da Silva (Pirajá). La Leishmaniose cutanée à Bahia.—*Arch. de Parasitologie.* 1912. Aug. 20. Vol. 15. No. 3. pp. 401–424. 5 plates.

This paper records the discovery of leishmania in eleven cases of cutaneous ulceration in Bahia, Brazil. The type of lesion is well shown in five excellent plates from photographs of the cases; in all there is a striking resemblance to oriental sore. One of the cases is described as having in addition to the cutaneous lesions ulceration in the nose and mouth, but the author did not examine these lesions for leishmania. The disease is evidently the same as that described by Carini and Paranhos, Lindenberg and Splendore. As in oriental sore the cutaneous lesions are limited mostly to the exposed surfaces of the body, but one patient had a sore on the abdomen near the umbilicus. In most the lesions were multiple, some being five centimetres in diameter. The author succeeded in obtaining flagellates in culture on one occasion, but was unable to keep the culture growing.

He attempted to inoculate animals with the disease but without success. Outside Bahia he encountered one case in Rio de Janeiro, where the disease has previously been noted by WERNER (*Kala Azar Bulletin* No. 2, p. 106). The patient was treated with intravenous injections of salvarsan and rapidly recovered. The paper, which is a long one, contains a historical account of the discovery of leishmania in South America and observations made by others on oriental sore.

C. M. W.

GALLI-VALERIO (B.). **Notes de Parasitologie. [iv. Sur un Cas de Bouton d'Orient chez un Persan.]**—*Centralbl. f. Bakt.* 1 Abt. Orig. 1912. July 17. Vol. 65. No. 4–5. pp. 307–308.

The author in this note mentions a case of oriental sore in a Persian. There were two sores on the face from which typical *Leishmania tropica* were obtained. Material from the sore mixed with citrate solution and incubated at 37° C. gave a culture in which the majority of the leishmania were unaltered but a few ovoid flagellate forms appeared. Scrapings from the sore were inoculated into the skin over the frontal region of a *Mus rattus*, which died seven days later. A small ulcer had formed at the site of inoculation and in smears from this the author claims to have found extracellular bodies of the type of *L. tropica*. Cultures and subinoculation of another rat from this sore were unsuccessful. A figure accompanying the paper shows two large macrophages containing leishmania.

C. M. W.

WENYON (C. M.). **Some Remarks on the Successful Inoculation of *Leishmania tropica* to Man.**—*Jl. London School of Trop. Med.* 1912. July. Vol. 1. No. 3. pp. 224–225.

The author inoculated himself by scarification with material obtained from an oriental sore in Aleppo, Syria. A suppurating wound developed and this healed under a scab. Six and a half months later, after he had returned to England, he suffered from fever and some intestinal disturbance, and there developed at the site of inoculation a small red papule. Shortly after two smaller papules appeared near the first. Leishmania were found in these papules. At the time of the original inoculation some material from the sore was placed on the uninjured skin where it was allowed to dry. No sore developed at this spot. Several deductions may be made from this experiment.—1. *Leishmania tropica* does not pass through uninjured skin. 2. The incubation period of oriental sore may be very long. 3. There was constitutional disturbance at the time of appearance of the papule. 4. The suppuration which occurred after inoculation was not sufficient to destroy the leishmania introduced. 5. It is possible that the purulent discharge from a suppurating tropical sore might be transferred to open wounds by auto-inoculation or by house flies and thus give rise to the disease.

C. M. W.

MALARIA.

Transmission.

Fermi (Cl.) & Lumbau (S.). **Können Anopheles-Mücken auf den Menschen Malaria übertragen, ohne sich durch Besuch von Malariakranken verseucht zu haben? Können dieselben sich die Infektion aus anderen Tieren als dem Menschen holen?** [Can Anophelines transmit Malaria to Man without having infected themselves from Malarial Patients? Can they infect themselves from Animals?]—*Centralbl. f. Bakt.* 1 Abt. Orig. 1912. July 3. Vol. 65. No. 1–3. pp. 105–112.

The experiments of Grassi, Bignami, and Bastianelli show it is improbable that mosquitoes become infected from animals with malarial parasites infective to man.

The authors' experiments were conducted over a period of three years.

(1) They allowed mosquitoes hatched in the laboratory to have their first meal on healthy men.

(2) Young mosquitoes were allowed to feed on animals obtained from malarial districts and then on human beings.

First series of experiments.—88 anophelines which had never previously bitten any man or vertebrate failed to cause malaria in 38 persons.

Second series of experiments.—(a) 26 anophelines which had fed on bats obtained from a malarious district were allowed to feed on 9 persons; no infection was noted. (b) 61 anophelines fed on malarious bats were allowed to bite three days later 21 persons; no infection took place. (c) 18 anophelines, fed on malarious bats and after a period of eight days allowed to bite 8 persons, did not cause infection. (d) 14 anophelines fed on malarious bats and after a period of ten days allowed to feed on 6 persons failed to cause infection.

Third series of experiments.—Anophelines (?number) were fed on infected bats, sparrows, owls, etc., and 10 days later on 26 persons. No infection took place.

Conclusions.—(1) Anophelines which have not fed on malarial patients are incapable of transmitting the disease to man.

(2) Anophelines which have fed only on bats, sparrows, owls, quails, and frogs obtained from malarious districts, cannot infect man with malaria.

J. G. Thomson.

Treatment.

Werner (H.). **Ueber Salvarsan bei Malaria nebst Bemerkungen über Zählungsmethoden von Malariaparasiten.** [Treatment of Malaria with Salvarsan.]—*Estratto dal volume 'In onore del Prof. Angello Celli, nel 25° Anno di Insegnamento'* 1912. pp. 291–297.

The author does not think that in salvarsan for malaria we have yet reached the ideal of a *magna therapia sterilisans* though its

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In the absence of Dr. David Thomson in Panama his place is taken by Dr. J. G. Thomson.

use has led to good results. The results obtained in simple tertian fever were most satisfactory; the rapidity of disappearance of the tertian parasites after an intravenous injection surpassed that obtained by the injection of quinine. The action of the drug is quite specific. The fever vanishes promptly; the gametes disappear as quickly as the schizonts, but the half-grown unsegmented parasites are more resistant. The author proved also the efficacy of salvarsan in vitro.

Altogether he has treated 33 cases. Among these there were six relapses, five of which he ascribes to an insufficient dose. In one case three doses were given before cure was obtained. Salvarsan is just as effective in quinine-resistant malaria as in those cases where there is no resistance; he has been able to cure such cases with the drug. No good results were obtained in the treatment of blackwater fever. The doses, given intravenously, were 0·5 gramme, repeated in 8 to 10 days. The results of the treatment of malignant tertian fever were not so satisfactory.

J. G. T.

JUSTI (K.). **Grundzüge der Malariatherapie.** [The Treatment of Malarial Fever.]—*Münch. Med. Wochenschr.* 1912. July 2. Vol. 59. No. 27. pp. 1505–1506.

The author believes that quinine is the most effective drug in malaria and that salvarsan is of little use. For oral administration quinine hydrochloride is recommended in the form of tabloids without coating, so as to secure rapid absorption, and he advises this method in all cases in which the digestive organs are unaffected. Tannate of quinine in chocolate is used in treating children.

NOCHT's method of giving separate small doses is preferred to that of GOLGI who administers 1 gramme, the latter method being of use only at certain stages of the infection. Quinine administered per rectum is regarded as useless, and subcutaneous injections are not recommended because of the frequency of abscess formation. The author, however, is a decided advocate of intramuscular injections. The form of quinine used was Quin. bimuriat. carbam. (Urea-quinine) in solution; in 2000 injections given intragluteally he observed only two cases of abscess formation, in each instance due to faulty technique. Intravenous injections were not tried.

The author refers to D. THOMSON's work on the leucocytes in malaria (see p. 22). His own researches have shown that the large mononuclears and the lymphocytes are increased in numbers at the expense of the polymorphs, and that during convalescence these gradually return to the normal. Any renewed fall in the number of polymorphs indicates a renewal of the infection, and as a rule is followed by a fresh attack of malarial fever. An absolute cure is only to be expected when the leucocyte index has become normal. As this never occurred in less than three months, this is considered to be the minimum period of treatment indicated. He admits, however, that continued blood examination is not always practicable.

J. G. T.

Prophylaxis.

Giemsa (G.) **Über die Vernichtung der Stechmücken mit Hilfe des Sprayverfahrens.** [The Destruction of Mosquitoes by Spraying.]—*Arch. f. Schiffs u. Trop. Hyg.* 1912. Aug. Vol 16. No. 16. pp. 565–567.

The author's fluid for destroying mosquitoes is composed as follows:—

Pyrethrum Tincture	580 grammes
Potassium soap of commerce (as far as possible odourless)	180 grammes
Glycerine	240 grammes

The cost of this fluid in flasks is about 2.38 marks per kilogramme. Purchase of larger amounts lowers the price.

Before application it is mixed with twenty times its volume of water. The fluid is sprayed about the room with a special pump, which is described. One person alone can use it. If a small room is to be sprayed, a hand pump may be employed. This mosquito fluid destroys also plant parasites without destroying the plant.

J. G. T.

Waldow (Dr.). **Chininprophylaxe oder mechanischer Malariaschutz.** [Quinine Prophylaxis or Mechanical Protection in Malaria.]—*Arch. f. Schiffs u. Trop. Hyg.* 1912. Aug. Vol. 16. No. 16. pp. 547–555.

The author points out the many difficulties in obtaining protection with mosquito nets and other mechanical devices. Quinine prophylaxis regularly carried out is simple and always possible. The drug is easily carried and enough to last a year with all its packing weighs only 100 or 200 grammes. Quinine also protects against relapses, but a net does not do so. Quinine is not sufficient to prevent infection, but it lessens it and makes it easy to deal with. In conclusion the author advises dwellers in the tropics not to depend on one method, but to use all that are practicable.

J. G. T.

Ryley (C.). **The Value of Quinine as a Malarial Prophylactic.**—*Jl. R. Army Med. Corps.* 1912. Sept. Vol. 19. No. 3. pp. 367–368.

Captain Ryley describes an interesting experiment which would appear to show that quinine in doses of five grains daily is not such an efficient prophylactic against malaria as is generally supposed. A white regiment had recently come from England to a malarial district in Hong Kong. To the men of A Company 5 grains of quinine was given daily. To the men of B Company no quinine was given.

Result:—A Company 47 per cent. infected with malaria.
B Company 49 per cent. infected with malaria.

The diagnosis was in every case verified microscopically.

The failure was not due to the deterioration of the quinine, for the same quinine was efficacious in therapeutic doses given to patients in the hospital.

David Thomson.

THOMSON (David). **The Destruction of Crescents: Conclusions regarding the Prevention of Malaria by the Administration of Quinine.**—*Ann. Trop. Med. and Parasit.* 1912. July 31. Series T.M. Vol. 6. No. 2. pp. 223–230.

The author still believes that quinine given in doses of 20 to 30 grains daily will reduce crescents to numbers below one per c.mm., within a period of three weeks. Methylene blue in doses of twelve grains daily has a similar effect. He believes that both these drugs destroy the crescents only indirectly, by destroying the asexual parasites from which they arise. He was unable to find that picric acid, in doses of six grains daily, had any appreciable destructive power either upon the asexual parasites or on the crescents. Soamin, X-rays, and "606" have no direct destructive action upon them, and apparently no direct means of destroying them has so far been discovered.

He disagrees with ZIEMANN, who thinks that the macrogametes are more resistant to quinine than the microgametes, as he found that during the administration of quinine, in doses of thirty grains daily, he was able to get flagellation in the crescents so long as crescents persisted. In one case flagellation was still found after fifteen days and in another after thirteen days. He concludes that the male crescents are quite as resistant to quinine as the female. Quinine and methylene blue, which are the most potent drugs against the asexual malarial germs, are also the best drugs for cleansing the system of crescents; so that a continuous quinine treatment for a month destroys not only the asexual, but also the sexual parasites.

Conclusions regarding quinine prophylaxis.—The author discusses the ideal methods of quininisation of a population, showing what science demands for the certain and rapid extinction of malaria by quinine alone. He finds fault with the continuous administration of five grains daily: (1) Because it is insufficient to prevent infection from mosquitoes; (2) Because it takes a long time to eradicate malaria from the system; (3) Because this dosage tends only to keep the disease latent in the system and may be favourable for the production of crescents.

He gives two alternative ideal methods, in which the amount of quinine taken annually is less in the aggregate than in the five-grain-daily method. He realises that these ideal methods are too exacting to be carried into practice; yet he points out that they are necessary to insure the eradication of malaria, if quinine alone is used.

His "Ideal Method A" is "That every adult person in the population (children in proportion, according to age) should take twenty grains of quinine daily and simultaneously for a period of three weeks, quarterly, *i.e.*, four times a year." He states that the administration of quinine in doses of twenty grains daily for

three weeks is almost certain to destroy both the asexual and sexual parasites. After this treatment the person will be non-infective to mosquitoes, and very few patients will have a tendency to relapse. Infective mosquitoes must necessarily become much fewer in number. No quinine is taken during nine months of the year. He thinks it is as practicable a method as the five-grain-daily method.

A more scientific method he calls "Ideal Method B." In this a quarterly blood census would be taken before the administration of the quarterly quinine. Only those who had parasites in their blood would require to take the three weeks' course of quinine, and those with crescents would, if possible, be isolated in mosquito proof hospitals till non-infective. He concludes by saying that these methods are ideal and, though they cannot be carried out to the letter in practice, should be considered in attempts to form systems of state medicine and sanitation in the tropics; and that the carrying out of these ideals even in part must necessarily do some good. "It is better to understand what is really required by science and, looking at the great difficulties of giving an effectual quinine prophylaxis, a simultaneous though partial mosquito reduction will probably be always required."

D. T.

LUSTIG (Alessandro). **Acht Jahre staatlicher Chininbetrieb in Italien und der Kampf gegen die Malaria.** [An Eight Years Quinine Campaign in Italy.]—*Münch. Med. Wochenschr.* 1912. Sept. 17. Vol. 59. No. 38. pp. 2053–2054.

It is stated that in Italy, before active measures were taken against malaria, the death roll due to the disease was about 15,000 per annum, and it was calculated that the total number of persons who suffered from the disease was about 2,000,000 persons per annum. Legislative methods were introduced in 1900, when the state made it easy for persons suffering from malaria to obtain proper treatment. Landlords and employers were compelled to treat their employees gratis. Prophylaxis was next aimed at, to effect which quinine was sold at the minimum cost and was produced as cheaply as possible. It was prepared by the State hospitals at the military laboratories in Turin and thus distant provinces could obtain regular supplies of the drug. The production of quinine is profitable to the state although it is sold cheaply, and the surplus is used for the free treatment of the poorer classes.

A table is given showing the fall in the death rate corresponding with the increased use of quinine.

J. G. T.

KÜLZ (L.). **Bemerkungen zu: A Treutlein "Verdient die Chininprophylaxe den Vorzug vor dem mechanischen Malariaschutz in den Tropen?"** [The Comparative Value of Mechanical and Quinine Prophylaxis in the Tropics.]—*Arch. f. Schiffs u. Trop. Hyg.* 1912. July. Vol. 16. No. 14. pp. 475–483.

The author discusses the two methods under three headings—Certainty of action; innocuousness; and practicability. He comes

to the conclusion that quinine prophylaxis is necessary to fill gaps in mechanical prophylaxis. To the question, Can such doses as are necessary be taken for a long time without harm? he replies that during his own sojourn in the tropics he has taken 600 grams of quinine and has had no illness except one of a surgical nature.

J. G. T.

Laboratory Studies.

Simpson (G. C.). **On Haemolysis in Malarial Fever. Preliminary Note.**—*Ann. Trop. Med. and Parasit.* 1912. July 31. Series T.M. Vol. 6. No. 2. pp. 231–233.

In the last eighteen months fifty cases of malaria in the Royal Southern Hospital, Liverpool, have been examined at various stages of the paroxysm and in the intervals, to discover if at any period a haemolytic principle could be discovered in the serum.

The blood was drawn into citrate solution and centrifuged in the pipettes, and the serum was separated from the corpuscles. The corpuscles were washed with normal saline, re-centrifuged, and made into a 5 per cent. emulsion. Non-malarial blood was similarly treated.

The following mixtures were used:—

Malarial corpuscles and malarial serum.
,, ,, ,, normal serum.
,, ,, ,, ,, ,, and malarial serum.
Normal ,, ,, ,, ,, ,, ,, ,,
,, ,, ,, malarial serum.
,, ,, ,, normal serum.

The mixtures were made each in one or two dilutions, incubated at 37° C., and examined after half an hour, one hour, and longer intervals. In no case did the control serum haemolyse the control corpuscles. In only one case did malarial corpuscles appear to be dissolved by control serum, and then only to a very slight extent. In no case did addition of control serum to malarial serum appear to modify the effect of malarial serum alone (Heated malarial serums were not tried). Only seven times out of one hundred observations did the malarial serum exert any haemolytic action, and in two of these it was extremely slight; in the other five cases definite haemolysis took place. Four of the five positive results were obtained in simple tertian fever, and only one in malignant tertian, though most of the cases examined were of the latter type. A very slight result was obtained in a case of blackwater fever.

Positive results appear most likely to be obtained in simple tertian cases at the onset of the paroxysm, when the young sporulating forms are set free in the blood. They are less easy to obtain in malignant tertian cases, in which the sporulation is spread over a larger period of time.

D. T.

THOMSON (David). **Further Observations on the Variations in the Number of Leucocytes and Crescents in Malaria.**—*Ann. Trop. Med. and Parasit.* 1912. July 31. Series T.M. Vol. 6. No. 2. pp. 215–221.

The author believes that the variations in the number of leucocytes, occurring in cases of malaria which have been apparently cured by quinine, are due to small numbers of parasites sporulating, but too scarce to be detected. The variation in the number of leucocytes commences about one to two weeks after the disappearance of the parasites. It is usually a quotidian or irregular variation, occurring about the time of day when the parasites previously sporulated. One seldom got a purely tertian variation in the number of leucocytes even in cases which had shown a pure tertian temperature, because even in apparently pure tertian cases of fever parasites will be found to sporulate between times, not sufficient in number to affect the temperature, but sufficient to cause a variation in the leucocytes.

From twelve experiments in which he injected varying numbers of malarial parasites (dead) subcutaneously, he was led to believe that a subcutaneous injection of ten to twenty million malignant tertian parasites caused a leucocytosis, whereas thirty to forty million and upwards caused a leucopenic effect as in a malarial paroxysm.

During a malarial paroxysm there is, as a rule, a leucopenia. Some observers have recorded a transient leucocytosis lasting about 20 minutes at the very commencement of the rigor. He has observed this only on two occasions, and thinks that it might be explained by the supposition that a very few parasites sporulate before the majority, and these few cause the temporary leucocytosis, which soon becomes a leucopenia when the majority sporulate. In cases of comatose malaria one frequently finds a marked leucocytosis during the fever paroxysm. He is unable to explain this exception.

Variation in the number of Crescents.—The author publishes a chart showing a tertian outburst of crescents into the peripheral circulation in a pure tertian case of *P. falciparum*. This chart also shows how quinine, in doses of thirty grains daily, gradually reduces the number of crescents to zero.

D. T.

CULTIVATION.

i. BASS (C. C.). **Successful Cultivation of Malarial Plasmodia.**—*Jl. Amer. Med. Assoc.* 1912. Sept. 21. Vol. 59. No. 12 (Pt. 1). p. 936.

ii. BASS (C. C.) and JOHNS (F. M.). **The Cultivation of Malarial Plasmodia (*Plasmodium vivax* and *Plasmodium falciparum*) in vitro.**—*Jl. Exper. Med.* 1912. Oct. 1. Vol. 16. No. 4. pp. 567–579.

The authors (ii) describe their technique for the cultivation of malarial plasmodia. Blood is drawn from the patient's arm

into a sterile glass syringe. Ten cc. of this are expelled into a defibrinating tube which contains one tenth of a cc. of a 50 per cent. solution of dextrose (Merck's). Gentle stirring with a glass rod is employed to defibrinate and the mixture is transferred to culture tubes, so as to form a column two inches deep. When the cells and parasites have settled there is half an inch to an inch of serum above the surface of the deposit. If the column is less than half an inch, the parasites often die before segmentation occurs. The plasmodia live and develop on the surface of the precipitated cells in a layer varying in depth from one fifteenth to one twentieth of an inch. All parasites below this die in from two to twenty-four hours. The incubation temperature should not be less than 40° C., and strict anaerobic precautions are necessary. The above technique is used to obtain the first generation of parasites.

If more than one generation are to be cultivated, the leucocytes must be removed by centrifugation. Culture tubes are prepared containing serum to a depth of at least half an inch, and red cells are planted at the bottom of these. In these leucocyte-free cultures it is possible, if fresh cells are planted at a suitable time, to obtain several generations of malarial parasites. The plasmodia develop and segment, and most of the merozoites enter new red blood corpuscles. The transplantation should be done within four or six hours of the time of maximum segmentation and, therefore, approximately every 48 hours for tertian and aestivo-autumnal parasites.

Serum from different individuals is not equally serviceable for the cultivation of malarial plasmodia. Leucocytes do not destroy the parasites as long as they are inside the red cells. Dextrose or maltose seem necessary. Blood drawn one or two hours after the patient had eaten a full meal was more serviceable for culture media than that drawn after long fasting. The most rapid growth is obtained at 41° C., and at this temperature aestivo-autumnal parasites will develop from the smallest rings and segment in about thirty hours. Calcium salts when added to cultures of aestivo-autumnal plasmodia caused haemolysis of the infected red blood corpuscles; from this it would seem that the presence of excess of calcium in the food or drinking water of a patient might possibly bring about haemoglobinuria.

The authors think that dextrose renders the red blood corpuscles less permeable to the destructive elements in the serum, and so the parasites are protected. Forms suggesting parthenogenesis have been observed in the cultures.

Positive cultures have been obtained from 29 cases of aestivo-autumnal malaria, from six cases of tertian malaria, and from one case of quartan. They have been carried on as far as four generations and, with proper attention to technique, could probably be continued indefinitely.

Summary.—" The asexual cycle of *Plasmodium vivax* and *Plasmodium falciparum* has been cultivated *in vitro* in human blood. The parasites have been grown also in red blood cells in the presence of Locke's solution, free of calcium chlorid and in the presence of ascitic fluid.

"The parasites grow within red blood cells and there is no evidence that they can be grown outside of these cells.

"The parasites are destroyed in a very few minutes *in vitro* by normal human serum or by all modifications of serum that we have tested. This fact, together with numerous observations of parasites in all stages of growth apparently within red cells, renders untenable the idea of extra-corpuscular development.

"Leucocytes phagocytize and destroy malarial plasmodia growing *in vitro* only when the parasites escape from their red blood cell capsule or when the latter is perforated or becomes permeable.

"Successive generations of *Plasmodium vivax* and *Plasmodium falciparum* have been cultivated *in vitro* by removing the leucocytes from the culture and by transplanting to fresh red blood cells and serum at proper intervals.

"The asexual cycle of *Plasmodium vivax* and *Plasmodium falciparum* cultivated *in vitro* does not differ from the same cycle growing *in vivo*.

"The sexual cycle has not been cultivated, though we have obtained some evidence of the possibility of its accomplishment.

"There can no longer be any doubt that *Plasmodium vivax* and *Plasmodium falciparum* are separate and distinct species. When grown in an identical culture medium and under exactly the same conditions they remain distinct.

"In twenty-nine cultures of aestivo-autumnal parasites many forms and sizes have been observed, so that evidence is supplied of the occurrence of different varieties of aestivo-autumnal malarial plasmodia. The so called tertian aestivo-autumnal variety may be seen at the proper stage in all cultures grown from merozoites.

"The form and appearance of the same culture of plasmodia may vary greatly under different conditions which are not necessarily destructive to the parasites. Their generation period may vary from thirty hours (aestivo-autumnal) to four days (tertian), as a result of variation in the temperature at which they were cultivated. Sexual parasites grow in the cultures and are more resistant to unfavourable conditions than schizonts, often living several days after the latter die out.

"Forms suggesting parthenogenesis have been observed."

J. G. T.

Miscellaneous.

Bisdom (Wijckerheld). **Einige Bemerkungen über die Malaria im Indischen Heer in den Jahren 1895–1909.** [Malaria in the Army in the Dutch Indies.]—*Janus.* 1912. July-Aug. Vol. 17. No. 7–8. pp. 400–409.

By means of a chart the author shows the remarkable diminution in the occurence of malaria both in Europeans and natives of the Netherland Indies. In 1886, 80 per cent. of the Europeans were affected, but in 1909 only 20 per cent. In natives in 1887 the percentage was 71; in 1909 this had fallen to 17. Since 1909 the fall has been rapid. In the same chart is given a graph of the percentage of beri-beri cases both in natives and Europeans, and this shows a similar falling off during these years. Many of the convalescent hospitals are now closed because of the scarcity of patients, and the chief reason for this improvement in health is the diminution of the cases of malaria. In 1885 the deaths due to malaria were 0·6 per cent.; in 1909, 0·07 per cent. The lessened death rate corresponds to the fall of cases of malaria and beri-beri. A table is given of the total deaths and also the deaths from malaria and beri-beri.

The cause of the great improvement in the general health is given as: improvement in hygenic surroundings; lessened use of

alcohol; day shelters for soldiers; quinine administration. The author does not think that gauze protection in the camps of the soldiers was very effective because the windows and doors were kept open; so that this could scarcely be assigned as the cause of the fall in malaria. He places the use of quinine as a prophylactic first. Quinine bisulphate is given in the form of sugar-coated tablets, made up in doses of 0·2 and 0·4 gram. These resist the climate better than the ordinary ones. At first they were expensive, but recently have been greatly cheapened.

The author in conclusion says that probably the use of quinine as a prophylactic and in treatment has been the most important factor in diminishing the incidence of malaria in the Netherland Indies.

J. G. T.

PRAMPOLINI (Bruto). **Contributo allo Studio dell Infezione Malarica in rapporto agli Interventi Operativi ed ai Traumi.** [Relation of an Attack of Malaria to Operations or Trauma.]—*Policlinico*, sez. prat. 1912. July 7. Vol. 19. No. 28. pp. 1009–1012.

The author points out that when the resistance of a patient is temporarily lowered by operation or trauma an attack of malarial fever, due to parasites lying latent in the body, may occur. Since he became head of the surgical department of the hospital at Cavarzere (Italy), it has often happened that after operations which were perfectly aseptic, *e.g.*, hernia, a rise of temperature occurred as high as 40° C. The presence of an enlarged spleen and, in some cases, of plasmodia in the blood enabled him to explain the temperature, which was intermittent, as due to malaria, and quinine always reduced this.

Similar attacks of fever were noted after fractures, dislocations, and severe contusions, and the author points out that even in the absence of a previous history of malarial fever in some cases he found the spleen enlarged and parasites present in the blood.

An account of nine cases is given. Five of these were operation cases, while four were accidents, in two of which operative intervention was necessary.

J. G. T.

POZZILLI (Pericle). **Sindrome Cerebellare Malarica.** [Cerebellar Symptoms occurring in Malaria.]—*Policlinico*, sez. prat. 1912. July 7. Vol. 19. No. 28. pp. 1012–1015.

The author points out that it is only during recent years that the nervous symptoms in malaria have been exactly described. He gives a detailed description of a case studied by him in Ferrara (Italy), which in his opinion presented a complete picture of the cerebral symptoms of acute malaria.

The patient was a boy aged 4 years. The parasites were of the aestivo-autumnal type and fairly numerous in the blood. Two crescents were found. The spleen was enlarged and anaemia was marked. The following phenomena were observed: disturbance of equilibrium; face expressionless; tendon reflexes exaggerated; intention tremor; scanning speech. Babinsky's sign was absent. There were no trophic changes, no Rombergism; sensibility was normal.

The author points out that the symptoms in this case indicated involvement of the cerebellum, as evidenced by the disturbance of equilibrium, etc. He thinks the presence of parasites in the cerebellar capillaries does not necessarily produce ataxia, but that the theory of Marchiafava, Celli and Bignami, namely that numerous punctiform haemorrhages are present, is more acceptable although it does not explain all cases. Marchiafava and Celli consider these small haemorrhages to be the cause of cerebral paralysis which does not give way promptly to treatment. Schupfer demonstrated them in the grey matter of the cerebellum. Bastianelli found at a necropsy slight atrophy of the cerebellum with remarkable diminution of Purkinje's cells.

Though in some cases of malaria the nervous symptoms are explained exclusively or partly by small haemorrhages into the cerebellar substance, malarial toxins may play a part and may even participate in the production of the haemorrhages. The author supposes that the vascular and perivascular lesions undergo sclerotic changes and that these become more marked in consequence of other disturbances, such as embolism, thrombosis and softening.

J. G. T.

Semple (David). **Some Remarks on a Criticism of Quinine Injection and Tetanus.**—*Jl. R. Army Med. Corps.* 1912. Sept. Vol. 19. No. 3. pp. 323–333.

In this article Sir David Semple defends himself against a criticism made by Major F. J. Palmer R.A.M.C. on his publication entitled "The Relation of Tetanus to the Hypodermic or Intramuscular Injection of Quinine." Semple quotes several paragraphs of the criticism, showing that his critic has failed to understand many of his experiments.

D. T.

Legrain (Emile). **L'Étiologie des Fièvres intermittentes.**—*Janus.* 1912. July-Aug. Vol. 17. No. 7–8. pp. 410–416.

The author appears to believe that the condition designated malaria is not caused by a protozoon, but is either a common gastro-intestinal infection or caused by a micrococcus which is a filter passer. Those interested should consult his paper.

A. G. B.

Malaria in Animals.

Leger (M.) et Bouilliez (M.). **Sur un Plasmodium des Singes. Passages par Espèces variées. Action pathogène.** *Compt. Rend. Soc. Biol.* 1912. Aug. 2. Vol. 73. No. 28. pp. 310–313.

The authors announce the discovery of a Plasmodium in the heart blood of a monkey (*Macacus cynomolgus*) which died in their animal house a week after arrival. They were able to carry this haematozoon through seven monkeys, and the rapid death of the animals showed that it was extremely pathogenic. The animals as a rule lived from 7 to 14 days after inoculation and the parasites were very numerous in the peripheral circulation. This

parasite resembles *Plasmodium inui* (Halberstaedter and Prowazek 1907) in its schizogony and in the absence of increase in size of the infected red blood corpuscles. Twelve to sixteen merozoites are formed. Sometimes the disease is more chronic; they have a monkey alive which has been infected for three months. The parasite was found to be pathogenic to several other species, namely *M. sinicus*, *Papio anubis*, *M. rhesus* and *Cercopithecus patas; Cercocebus fuliginosus*, the chimpanzee, and the maki of Madagascar proved refractory. The authors at present do not think there is enough evidence to form a new species, since the pathogenicity may have been caused by the lowered resistance of the monkeys, which were kept in a cage in Paris. They will make inoculation experiments with other monkeys.

J. G. T.

SERGENT (Etienne et Edmond). **Paludisme des Oiseaux** (*Plasmodium relictum*). **L'Infection peut se faire par simple frottis du Thorax du Moustique sur la Peau.**—*Compt. Rend. Soc. Biol.* 1912. July 12. Vol. 73. No. 25. p. 36.

The authors were able to infect four out of ten canaries with bird malaria by simply rubbing the crushed thoraces of infected mosquitos into a scratch on the exposed skin. The incubation period was ten to twelve days. All the control canaries (100 per cent.) bitten by infected mosquitos contracted the disease, and the incubation period in them was shorter—viz.: six to nine days.

J. G. T.

MOLDOVAN (J.). **Ueber die Immunitätsverhältnisse bei der Vogelmalaria.** [Immunity in Bird-Malaria.]—*Centralbl. f. Bakt.* 1 Abt. Orig. 1912. Aug. 24. Vol. 66. No. 1. pp. 105–110.

Plasmodium praecox, the author writes, is very closely allied to the parasite which causes malaria in man. As long as a bird is infected with parasites it appears to be resistant to a new infection, but the moment it has recovered the power of resistance is lost. He tried to find out if there was an antibody in the blood. (1) He took the serum of a chronically infected bird and kept it in contact with the injection material, but no protective action resulted; (2) He looked for complement fixation phenomena in the blood of sick canaries and found none; (3) An animal which had been ill for a long time and had recovered was not immune to a new infection.

The author shows that a canary infected with *Plasmodium praecox* may in a short time completely recover; in the majority of cases, however, the disease proceeds to a characteristic chronic infection. By the injection of a chronic case with the blood of a different animal relapses were obtained after an interval of about eight days.

The author gives a full set of experiments and a table too long for insertion; those interested are referred to the original article.

J. G. T.

BLACKWATER FEVER.

ACHARD (Ch.) and SAINT-GIRONS (F.). **Fièvre Bilieuse Hémoglobinurique. Remarques sur la Pathogénie de l'Hémoglobinurie.**—*Bull. et Mém. Soc. Méd. des Hôpit. de Paris.* 1912. June 6. ser. 3. Vol. 28. No. 19. pp. 749–758.

The authors give a very full description of a case of blackwater fever with biliary symptoms occurring in Paris. The haemoglobinuria did not occur till the patient entered hospital.

A lady, age 37, entered hospital complaining of pain in the region of the appendix. She had lived several years on the West Coast of Africa (Gulf of Guinea) and also in the Sudan, and gave a history of several attacks of malaria. On her admission her temperature was 38·2° C., and she received half a gramme of quinine with an equal quantity of antipyrin. Next day a dose of 1 gramme of quinine was given. On the following morning marked jaundice was noticed and a very intense haemoglobinuria. Anaemia was profound. In spite of treatment the patient succumbed after a short illness of about five days. No autopsy was performed. Examination of the patient's blood during the attack of haemoglobinuria showed no haemolytic power in the serum. The authors describe their technique. The blood counts showed a severe anaemia. The leucocytes rose gradually during the five days of illness from 9,200 per cmm to 60,800 per cmm. No parasites were found in the blood. The serum was examined for urea on two occasions. It contained 0·53 grammes per 1,000 on the first examination, and 2·04 gramme per 1,000 on the second. The urine contained debris of red blood corpuscles and haemoglobin. The vomit contained bile and urea (1·50 grammes to 1·27 grammes per 1,000).

The authors allude to the classical opinion that haemoglobinuric fever is due to the presence of haemoglobin free in the serum. This opinion is based on the observations of BOUFFARD and ZIEMANN, who found haemolytic power in the serum and abundance of haemoglobin in the urine without notable sediment of red blood corpuscles. In the authors' own case the serum showed oxyhaemoglobin in one examination on the first day, but on the other hand the plasma collected in sodium oxalate solution had no haemolytic power, nor had the serum either for the patient's own corpuscles or for the corpuscles of two normal individuals. Coagulation was normal. They compare this case with one of typhoid fever, which developed haemoglobinuria. At the post-mortem renal haemorrhages were found. The urine contained haemoglobin and also debris of red blood corpuscles, but the serum had no haemolytic action.

After a comparison of this and their blackwater case they conclude that the haemolytic action is in the urinary tract or in the kidney.

J. G. T.

CARDAMATIS (Jean P.) **Les Hémoglobinuries chez les Paludiques commes celles occasionnées par la Consommation des Fèves fraîches peuvent-elles être des Phénomènes de l'Anaphylaxie ?**—*Bull. Soc. Path. Exot.* 1912. July. Vol. 5. No. 7. pp. 521–523.

The author believes that haemoglobinuria is not a disease but rather a symptom, perhaps a phenomenon of anaphylaxis. Quinine is not an albuminoid substance, and would appear not to be able to produce this phenomenon; it combines however with the albumen of the stomach, and is absorbed as an albuminate of quinine. On this account and perhaps also owing to digestive disorders quinine, entering into the system of a malarial subject through the stomach, might be able under certain conditions still unknown, to act as an antigen. This antigen combined with the malarial toxin produces antibodies which provoke a sensitiveness to quinine in the malarial subject, so that every further dose of quinine produces the phenomenon of anaphylaxis, perhaps on account of its combining with the antibodies produced or perhaps by its transformation into a hypertoxic material.

Although the clinical symptoms of an anaphylactic attack accord only partially with those of an attack of blackwater, yet no one can explain the latter any better than by the supposition that it is similar to the haemoglobinuria following upon the consumption of the pods, leaves or flowers of fresh beans. The anaphylactic phenomena produced by green beans are probably due to the introduction into the system, on account of faulty digestion, of a vegetable albuminoid, foreign to the system, which acting as an antigen, *i.e.*, as toxic material, excites the formation of antibodies, and following upon this the condition of anaphylaxis.

D. T.

LEISHMAN (Wm.). **Cell-Inclusions in the Blood in Blackwater Fever.** Second Note.—*Jl. R. Army Med. Corps.* 1912. Aug. Vol. 19. No. 2. pp. 151–156, with 4 figs.

In the *Journal of the Royal Army Medical Corps* (Vol. 18, No. 5, May 1912, pp. 493-504) Sir Wm. Leishman recorded the occurrence of cell-inclusions in certain of the large mononuclear cells found in peripheral blood films of a case of blackwater fever which occurred in Uganda. He suggested the possibility of these bodies being parasites of a chlamydozoal nature. He now describes the occurrence of similar bodies in the peripheral blood films of two further cases of blackwater fever, which he records as "Case 2" and "Case 3" respectively, that dealt with in his first note being alluded to as "Case 1."

Case 2 was a native boy suffering from blackwater fever in one of the outlying mines of the Rand, S. Africa. The blood film showed an intense degree of leucocytosis, but he had no record of the actual blood count. The differential count showed 2·0 per cent. of "chrome cells." Very large numbers of nucleated red cells were present, in the proportion of one megaloblast and four normoblasts to every 100 white cells. He states that "this blood

picture makes it evident that the bone marrow in this case was gravely affected, a sign-post which might possibly indicate a useful path of exploration in the future." The cell inclusions, described in 'Case 1' were found to be plentiful in this film. They occurred only in the endothelial type of cell, and none was found in any of the ordinary leucocytes found in normal blood. The type of inclusion most commonly met with was that figured in Nos. 1 to 4 of the plate. They stained a varying depth of pink or red, and were almost invariably clear cut and circular in contour. The forms were mostly homogeneous. The ring forms which he described in Case 1 were scarce in this case, and he was unable to find any of the large forms found in Case 1.

He states that he had great difficulty in deciding whether these inclusions might not be altered or fragmented red cells which had undergone phagocytosis, but he still considers that the inclusions are not explicable on this ground. In Case 2 as in Case 1, he found that many of the mononucleated cells contained numerous granules in the cytoplasm, which he was unable to refer to any of the types of EHRLICH or to the azure granules of normal lymphocytes or hyalines. These granules were deep red, larger than neutrophile granules, but not nearly so large as coarse eosinophile or basophile granules. Their distribution in the cell cytoplasm was scanty. These granules were never seen in polynuclears or eosinophiles. He suggests that they may possibly represent a stage in the history of a chlamydozoan.

In this case and in Case 3 he found certain curious cells which he had never previously encountered, either in blood-films or in plates illustrating cytological work. These cells were not uncommon and could be readily distinguished from all others by the deep chromatin tint of the whole cell; they were of the size of ordinary polynuclears and their nuclei were sometimes of that type, sometimes mononuclear. The cytoplasm appeared more or less completely filled with material which showed the chromatin reaction and, in almost every instance, the red colour was most intense at the periphery, giving the cell an appearance of being capsulated. In other instances the partial disruption of the cell permitted it to be seen that the red-staining material consisted of a mass of chromatin bodies, sometimes of quite irregular shape and size, but occasionally showing a tendency to ring form (see accompanying plate, figs. 1 and 2). He calls these cells "Chrome Cells."

Case 3.—Two blood films from a case of blackwater fever described by ROSS, THOMSON and SIMPSON in the *Annals of Tropical Medicine and Parasitology* (Vol. 4, p. 308, 1910). These films were taken at the commencement of the third attack of fever, during which there was no haemoglobinuria and no malaria, parasites were found. On the day on which these films were taken the leucocyte count was 3,000 per c.mm. The differential count showed 0·5 per cent. of "Chrome Cells." These are shown in figs. 3 and 4. The one depicted in fig. 4 has ruptured and shows chromatin rings, which the author thinks are identical with the cell inclusions which he has been describing.

FIG. 1.

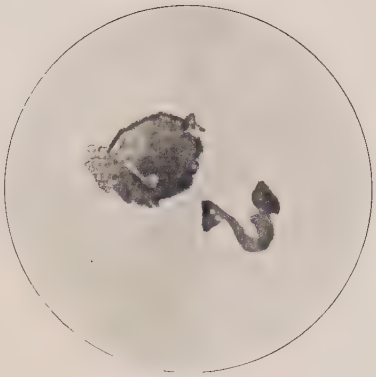

FIG. 2.

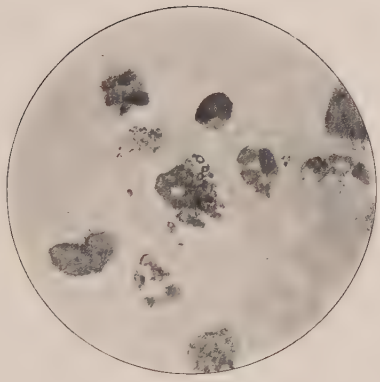

FIG. 3.

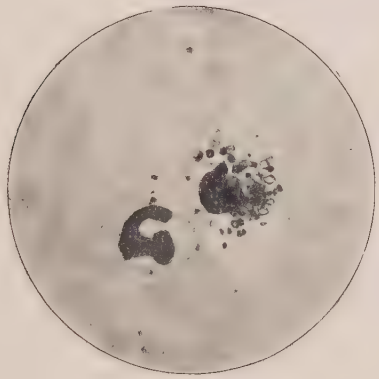

FIG. 4.

To illustrate Sir WM. LEISHMAN'S paper on "Cell-inclusions in the Blood in Blackwater Fever."

[Reproduced by permission from the *Journal of the Royal Army Medical Corps.*]

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He thinks that the cell inclusions described by Low in some fever cases from Borneo and in the blood of some pellagrins are not identical with those found by him in these three cases, but states that his cell inclusions are identical with those found in the blood film of a case of chronic malaria from Nigeria shown to him by Major HARRISON. This case had no history of blackwater fever, but the author thinks it significant that the fever was contracted in a blackwater fever country.

D. T.

The Occurrence of Blackwater Fever in the Nyasaland Protectorate, Northern Nigeria and Sierra Leone. [From the Reports of Medical Officers sent during June, July, and August, 1912, to the Secretary of State for the Colonies].

From Nyasaland nine cases of blackwater fever are reported by Drs. J. B. DAVEY, R. BURY, A. G. ELDRED, and H. S. STANNUS. Several of the patients gave a definite history of previous malarial attacks, and two are reported to have used quinine at irregular intervals.

From Northern Nigeria Dr. F. MANNING, Acting P.M.O. reports eight cases, and of these three only stated they were regular in the use of quinine; he thinks however there is some doubt whether they really did take the regulation daily 5 grain dose recommended by the authorities. In this report is given the seasonal incidence of this malady from the year 1898 to 1911.

From Sierra Leone Dr. R. M. FORDE reports seven cases. All, as far as he can remember, occurred in persons of some length of service in West Africa, who never took quinine regularly as a prophylactic. Dr. Forde has always noted two well-marked types: (*a*) a severe class of case, with rapid onset; (*b*) a milder class of case, with slower onset, no relapses, and with rapid recovery.

J. G. T.

RELAPSING FEVER.

Transmission.

Nicolle (C.), Blaizot (L.) et Conseil (E.). **i. Etiologie de la Fièvre Récurrente. Son Mode de Transmission par le Pou. ii. Conditions de Transmission de la Fièvre Récurrente par le Pou.** —*Compt. Rend. de l'Acad. Sci.* 1912. June 10. Vol. 154. No. 24. pp. 1636–1638: and Aug. 26. Vol. 155. No. 9. pp. 481–484: also (i) in *Arch. Inst. Pasteur Tunis.* 1912. No. 3. pp. 110–112.

Although various investigators have been struck by the analogies between relapsing and typhus fever and from an epidemiological point of view have arrived at the opinion that the louse is responsible for the transmission of relapsing fever, Nicolle, Blaizot and Conseil are the first to succeed in proving experimentally the truth of this hypothesis.

The Algerian strain of relapsing fever was employed throughout these experiments and the authors first attempted to infect both monkeys (*Macacus*) and men by the bites of body-lice (*Pediculus vestimenti*) that had previously fed on infected blood (*i.e.* in which spirochaetes were present). Although numerous experiments were made, and in one case no less than 4,707 infected lice were allowed to feed on one man, none of the men or animals ever became infected with spirochaetosis or showed any rise in temperature. The monkeys used in these experiments were subsequently proved to be susceptible to the disease by the inoculation of small quantites of infected blood. In every case the lice were merely allowed to feed on the animal and then removed, and the results clearly show that under these conditions the bite of infected lice is innocuous.

On examination of the crushed contents of lice that had just fed on an infected animal numerous living spirochaetes were found. When the lice were kept at a temperature of 28° C. these spirochaetes disappeared after one day, but often reappeared, in one series between the 6th and 8th day and in two other series between the 11th and 12th day. An eighth of the lice employed, both the body louse and *P. capitis* (the head louse), was found to show spirochaetes on the ninth day, and their virulence was proved by inoculating them into monkeys, which invariably became infected. Moreover, the authors found that when an emulsion of two body lice that had fed on an infected monkey nine days previously was rubbed on the slightly excoriated surface of the skin of a man, he became infected with relapsing fever five days later. In another case, in which an emulsion of an infected louse was placed on the conjunctiva, the patient showed spirochaetes after an incubation period of seven days. Both these cases were cured on the first day of infection by an injection of salvarsan.

The method in which infected lice may transmit Algerian relapsing fever is as follows:—When a man is bitten by a louse the irritation produced usually causes him to scratch that part of the skin, and thus the parasite is often crushed on to the skin and its contents get on to the finger-nails. The excoriation of the skin produced by the scratching is sufficient to allow the entry of the spirochaetes present in the body of the louse and

thus infection occurs. The mere bite of the louse, however, is innocuous, as shown in the above described experiments.

Finally a most important fact, also demonstrated by these authors, is the hereditary transmission of infection in the body-louse, which proves that this insect is a true intermediate host for the spirochaete.

Eggs were laid by the lice 12-20 days after they had fed on an infected monkey. These eggs were kept in a moist chamber at 28° C. and commenced to hatch out 17 days later. Some of these young lice and also some eggs were inoculated into a monkey; 10 days later this animal became infected with spirochaetosis.

ii. This paper contains some important additions. The authors attempted to determine how long the lice remained infected and also when the spirochaetes finally disappeared from the insect's body. It was found that after an infective feed the spirochaetes never reappeared in the lice earlier than the eighth day; that they persisted as late as the nineteenth day, but never later. A monkey inoculated with 24 lice on the twentieth day did not become infected. [The authors leave one to assume that for the production of infection the presence of spirochaetes, *as such*, in the body of the lice is necessary, but this is not stated.]

As the results of experiments it was found that of 165 lice (♂ and ♀) 29, or 17·57 per cent., became infective, proportionately four times as many females as males; the former therefore seem to be more susceptible. A few experiments with the head louse gave approximately similar results to the above, so that the species of Pediculus employed seems to be unimportant.

The spirochaetes have never been seen in any other site than the coelomic fluid of the louse. They were never found in the eggs dissected out of the ovaries of infected lice. The contents of the digestive tube are uninfective and also the faeces, as tested by inoculations into monkeys.

Another example is given of the innocuity of the mere bites of infected lice, for one subject allowed himself to be bitten 6,515 times by lice that had fed on an infected monkey. Of these 1,918 were between the eighth and nineteenth days, when the coelomic fluid of many of them was swarming with spirochaetes, which on the slightest excoriation were capable of producing infection.

The hereditary transmission of the infection is now considered to be unusual, for the authors have failed to repeat this in two successive cases, when large numbers of young lice from infected parents were inoculated into monkeys.

Attempts were made to transmit the spirochaete by means of *Ornithodorous savignyi* obtained in Tripoli, but neither the bites of ticks that had fed on infected animals, nor the inoculation of the tick contents into monkeys was followed by infection.

[These results are of the highest importance, for although many doctors have suggested that lice, especially the body-louse, *P. vestimenti*, were responsible for the transmission of various relapsing fevers, previously all attempts to obtain experimental

evidence had failed. We now have an excellent example of what may be termed the "contaminative" mode of infection by the intermediate host and it is interesting to compare it with the transmission of *S. duttoni* by *Ornithodorus moubata*. In this case both LEISHMAN and HINDLE have shown that the tick produces infection only as a result of the entrance of the infective faeces into the wound caused by the tick's bite. In both cases, therefore, the contaminative mode of infection takes place and thus the transmission of these two different varieties of spirochaetes is essentially the same.

After the results of LEISHMAN, BALFOUR, and HINDLE, on the changes undergone by blood spirochaetes in the intermediate host, it is not to be expected that spirochaetes, as such, would be found in the eggs from the ovary. The intracellular coccoid bodies are never mentioned and do not seem to have been looked for. The inoculations of this phase are always somewhat uncertain and, consequently, the negative results obtained by the inoculation of eggs from the ovary of an infected louse are inconclusive.]

Edw. Hindle.

CHEMOTHERAPY.

HERMANT (Dr.). **Note sur la Fièvre Récurrente dans la Province de Nghê-An.**—*Bull. Soc. Méd. Chir. de l'Indochine.* 1912. Vol. 3. No. 7. pp. 418–426.

MOUZELS (P.) et NGUYÊN-XUAN-MAI. **Note sur 373 Cas de Fièvre Récurrente traités au Lazaret de Hanoi par le 606 au Cours de l'Année 1912 du 1er Janvier au 1er Juin.**—*Ibid.* pp. 427–435.

LEGENDRE (J.). **Traitement de la Fièvre Récurrente par l'Arsénobenzol.**—*Bull. Soc. Path. Exot.* 1912. June. Vol. 5. No. 6. pp. 339–342.

All these papers describe the result of treating the relapsing fever of Tonkin with arsenobenzol (salvarsan), and in each case the authors agree that this drug is an excellent specific for the disease.

LEGENDRE gives the results of treating 8 cases with 0·2-0·3 gms. arsenobenzol; in every patient the spirochaetes disappeared within 24 hours and no relapse occurred.

HERMANT treated 51 patients by means of intravenous injections of 0·12-0·20 gms. of arsenobenzol and in each case the spirochaetes disappeared after a few hours and there was no relapse. One patient received the drug subcutaneously, and an abscess formed at the site of injection; this method therefore was abandoned. In four other cases the infection was followed by the death of the patients, but three of these were old men aged respectively 60, 63 and 70 years, for whom there was no hope of recovery, whilst the other was an anaemic woman 36 years old. His supply of arsenobenzol being exhausted, Dr. HERMANT injected 9 patients with atoxyl, but the drug merely produced an exaggeration of the fever.

The most important results are those of MOUZELS and NGUYEN-XUAN-MAI. Forty-one patients were treated by intra-rectal injections of arsenobenzol; the others received the drug intravenously. The intra-rectal method was found to be both inconvenient and less prompt in its action; moreover, as double the dose is necessary, it is more expensive. Its method of application is as follows:—The contents of the rectum are washed out by means of an injection of 500 cc. of boiled water, and 0·20-0·40 gms. of the drug, dissolved in the same way as for intravenous injection, are introduced into the rectum as high up as it has been emptied. The method is recommended only for children and patients in whom it is difficult to find the veins. Of 332 patients treated by intravenous injections (usually 0·20 gms.) only 6 relapsed and these were all cured by a second injection. The administration of the drug is usually followed by a rise in temperature and an aggravation in the general state, but after 8-18 hours these symptoms disappear and recovery is so rapid that within 4-5 days the patient is quite well.

In 24 cases, about the 12th day, they observed a febrile relapse without the appearance of spirochaetes. This so-called "Rebound Fever" is not affected by '606.' It usually lasts only 24 hours, but occasionally as long as three days.

Although 22 of the patients died in the hospital, in only four cases was death due to the relapsing fever and in these the state of health was so precarious that all died within two or three days of entrance. Spirochaetes were not present in the circulation at the time of death. Before '606' was employed the mortality from the disease was 4·16 per cent. in this hospital, but since the introduction of this specific it has been only 1·07 per cent. In addition to diminishing the mortality it lowers the duration in hospital by more than two-thirds and thus is very economical.

All these authors agree as to the excellent results obtained by the use of "606" as a specific for the relapsing fever of Tonkin; intravenous injections are found to be the most satisfactory. The dose is generally about 0·20 gms. for an adult Annamite.

To his clinical notes Dr. Hermant adds some observations on the epidemiology of the fever and comes to the conclusion that the body-louse is probably responsible for its transmission.

E. H.

CONSEIL (E.) et BIENASSIS (E.). **Traitement de la Fièvre Récurrente par le Néosalvarsan d'Ehrlich.**—*Bull. Soc. Path. Exot.* 1912. July. Vol. 5. No. 7. pp. 476–481. With 3 charts.

Although these authors obtained good results by the treatment of North African relapsing fever with salvarsan (intravenous injections of 0·008 gms. per kilo.) and cured ten cases out of eleven with one injection, the dangers of the treatment caused them to try other compounds. As a result of the treatment of nine cases with neosalvarsan they recommend this medicament. The temperature charts of three of these cases are given. In addition to its perfect solubility and the ease with which it can be manipulated it is found to be much less toxic than arsenobenzol (salvarsan); for in one case the injection of 1·45 gms.

of neosalvarsan into a patient weighing 60 kilos (·025 gms. per kilo.) did not produce any ill effects. This inferior toxicity permits the use of this new compound in severe cases of relapsing fever when the state of the liver prohibits the use of the older specific. Finally, the authors are of the opinion that the injection of neosalvarsan is followed by a much less severe reaction than that which follows the injection of salvarsan.

E. H.

CASTELLI (G.). **Chemotherapeutische Versuche über die Wirkung des Kakodyl und Arrhenal bei experimentellen Spirillen- und Trypanosomenerkrankungen.** [Chemotherapeutical Study of the Action of Cacodyl and Arrhenal on Experimental Infections of Spirochaetes and Trypanosomes.]—*Arch. f. Schiffs u. Trop. Hyg.* 1912. Sept. Vol. 16. No. 18. pp. 605–619.

The author finds that sodium cacodylate and arrhenal are without any effect on infections of *Spirochaeta recurrentis* in mice, *S. gallinarum* in fowls, and *Trypanosoma brucei* in mice. Moreover, these compounds had no effect on scrotal infections of *Treponema pallidum* and *T. pertenue* in rabbits. Even when the maximum doses were administered, both intravenously and intramuscularly, no parasiticidal action was noticed. Castelli concludes, therefore, that sodium cacodylate and arrhenal are of no use for the treatment of spirochaetal infections.

Comparing the effect of salvarsan, which is well known to possess very strong parasiticidal properties in the above infections, the author accounts for the different properties of these arsenical compounds by their respective chemical constitutions. In both sodium cacodylate $\left(\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>As<\!\!\begin{matrix}O\\ONa\end{matrix}\right)$ and arrhenal $\left(CH_3{-}As<\!\!\begin{matrix}O\\ONa\\ONa\end{matrix}\right)$ the arsenic atom is pentavalent, whereas in salvarsan, the arsenic is in the trivalent form. In addition, the latter compound contains the (OH) in the para position and the amido group (NH_2) in the ortho position, and both of these groups are chemically very active.

E. H.

SCHILLING (Cl.), VON KROGH (M.), SCHRAUTH (W.), and SCHOELLER (W.). **Die Wirkung organischer Quecksilberverbindungen bei Spirochäteninfektionen. (1. Mitteilung).** [The Action of Organic Mercury Compounds on Spirochaete Infections. Part I.]—*Zeitsch. f. Chemotherapie.* I Teil. Originale. 1912. Vol. 1. No. 1. pp. 21–43.

The authors have studied the action of a number of organic mercury compounds on spirochaetes, mainly with the object of determining the manner in which the respective compounds were effective. At first they employed fowls infected with *S. gallinarum*, but it was found that this infection was very uncertain in its reactions. Accordingly, in all subsequent experiments they employed mice infected with a very virulent strain of *S. recurrentis*.

An interesting series of preliminary experiments was performed on the properties of this strain. It was found that the virulence of the spirochaetes depended largely on the stage of the infection. Thus, mice that were injected with the blood of another animal the first day of infection lived distinctly longer than mice injected from the same animal on the second day, the average duration of life in the first case being 3·1 days and in the second 1·8 days. On the other hand those injected on the third day of the infection lived on an average 3·8 days, *i.e.*, slightly longer than those of the first day. The authors explain this diminution of virulence on the third day of the infection as the result of the antibodies present in the blood, which are injected together with the spirochaetes. The virulence of the strain was increased, until 24 hours after injection a mouse shewed 50-100 spirochaetes in each microscopic field. This strain was employed in all subsequent investigations of the effects of the mercurial compounds.

In addition, the authors seem to shew by the following experiment that spirochaetes produce toxins:—The blood of five heavily infected mice was mixed with 2 per cent. citrate-broth, the blood cells were removed by the centrifuge, and the remaining serum, *containing spirochaetes*, heated for one and a half hours at 45° C. This serum was then more strongly centrifuged in order to carry down the spirochaetes, and then divided into two parts. The blood of normal mice was also treated in a similar manner to the above, being mixed with 2 per cent. citrate-broth, centrifuged and then heated for one and a half hours at 45° C.

Mice were then injected with:—(1) The warmed serum from normal mice; (2) the serum from infected mice prepared as above described; and (3) the mass of dead spirochaetes carried down by the second centrifugation. All the mice died as a result of the injections, but the length of life averaged 4·5 days for the normal serum (1) and 5 days for the spirochaete serum (2). Thus under these conditions normal mouse serum becomes toxic for mice. On the other hand those injected with the dead spirochaetes (3) died on an average in 4·1 days, thus suggesting that these parasites contain toxic substances.

As a result of their researches on the effect of mercurial compounds on the virulent strain of *S. recurrentis*, the authors come to the opinion that these medicaments only act indirectly on the infection. The latter seems to affect chiefly the alimentary canal of infected mice, causing enteritis, and the mercurial compounds mainly act by combating these symptoms. Their action, therefore, is quite different to that of salvarsan, which directly kills the parasites without affecting the organs. The mercurial compounds are more organotropic than parasitotropic and act indirectly through the organs of the body. In addition, it is probable that these compounds have a stimulating effect upon the production of antibodies and in this way also indirectly affect the parasites.

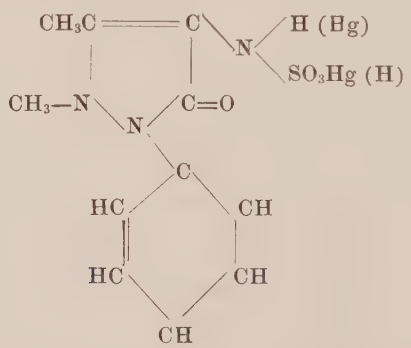
Of the numerous groups of mercury compounds which were tested only a few of the phenol derivatives were found to be relatively efficacious and in all these the Hg. was attached to the benzine ring by one valency only.

E. H.

KOLLE (W.), ROTHERMUNDT (M.) and PESCHIÉ (S.). **Untersuchungen über die Wirkung von Quecksilberpräparaten auf Spirochätenkrankheiten. I. Chemotherapeutische Wirkungen der Hg-Verbindungen und im besonderen eines neuen, stark auf Spirochäten wirkenden organischen Hg-Präparats von sehr geringer Giftigkeit.** [The Action of Hg Preparations on Spirochaete Infections, especially that of an Organic Compound of very low Toxicity.]—*Deut. Med. Wochenschr.* 1912. Aug. 22. Vol. 38. No. 34. pp. 1582–1585.

This paper contains an account of studies on the biological action of certain mercury compounds, especially those which are used in the treatment of syphilis, and of a new compound—Mercuric-sulphamino-dimethyl-phenyl-pyrazolone. The parasiticidal properties of the drugs were tested by their action on fowl spirochaetosis and their respective toxicities in both fowls and rabbits. As the result of an examination of the properties of a number of compounds very interesting relations were found to exist between the chemical constitution and the therapeutic properties. It was found that the simple mercuric salts of the aliphatic series are very inferior to organic mercury compounds containing either the benzine ring or the pyrazolone nucleus. In the two latter not only is there a considerable diminution in the toxicity, but also the relation between the *Dosis curativa* and *Dosis toxica* is much more favourable.

A suitable mercurial compound should possess strong parasitotropism with slight organotropism, so that it is quickly eliminated from the body. The authors find that the sulphamino group reduces the organotropism without affecting the parasitotropism; and that the latter property is increased if the Hg. is attached to a pyrazole nucleus and not directly to a benzine ring. E. SCHEITLIN has prepared a mercurial compound combining these qualities and this has been found to give the best results in the treatment of fowl spirochaetosis. The compound is known as mercuric-sulphamino-dimethyl-phenyl-pyrazolone and has the following constitution—



For this compound the relation $\frac{\textit{Dosis curativa}}{\textit{Dosis toxica}}$ is less than 1/100, which compares very favourably with that of Hermophenyl (1/60), from this point of view the next best organic mercury

compound. The authors accordingly recommend that this new Hg. preparation should be used in conjunction with salvarsan in the treatment of syphilis.

E. H.

LEVADITI (C.). **Intervention de l'Organisme dans la Guérison médicamenteuse des Maladies à Spirilles.**—*Bull. Soc. Path. Exot.* 1912. July. Vol. 5. No. 7. pp. 524–544. With 9 curves.

The present memoir is to some extent a summary of the previous work of the author, both alone and with various collaborators, on the mode of action of organic arsenical compounds on spirochaetes and trypanosomes. It also includes the accounts of experiments on the treatment of infections of *Spirochaeta duttoni* in rats by '606.'

Briefly stated, the author's conclusions are that in this disease the nearer one approaches the crisis before administering the medicament, the more quickly the parasites disappear and the less of the compound is necessary in order to effect this disappearance. In other words, the quickness of the sterilization of the blood of an infected animal is inversely proportional to the time which separates the moment of injection from what would have been the natural crisis of the infection. For example, a number of rats were infected with a strain of *S. duttoni* in which the first attack lasted four days. These rats were respectively injected with equal quantities of '606' at various times on the second and third days of the infection. Those injected on the beginning of the second day of the infection were not free from spirochaetes until 33 hours later, whereas in the case of the rats treated in the afternoon of the third day the spirochaetes disappeared in three and a half hours. In addition to this, it was found that a relatively rapid cure could be obtained by the use of smaller doses of the medicament if one was careful to administer the salvarsan during the course of this "precritical period" of the spirochaetal infection.

These results are only applicable to those parasitic diseases which terminate spontaneously with a crisis. They are not applicable, for example, to rats infected with *Trypanosoma brucei*, for in this case the disease is only terminated by the death of the animal and there is no spontaneous crisis.

Further proofs of the fact that "606" acts only in conjunction with the organism are the results obtained by the treatment of rats that had previously been vaccinated by the injection of spirochaetes killed by heating to 56° C. The rats which had been thus prepared were subsequently infected with spirochaetes and injected with "606" on the second day of infection. The parasites disappeared as quickly in these rats as if the drug had been injected on the third day, just before the crisis.

As for the mechanism of these phenomena two hypotheses are possible:—In the first case one can suppose that as the disease approaches the crisis the parasites become reduced in vitality and are more susceptible to the drug. The results of treating "prepared" rats on the second day of infection, which is far from the crisis, are strong arguments against this hypothesis. Again, if one takes the blood of an infected rat on the

third day of infection, inoculates it into another rat, and immediately follows the inoculation by an injection of "606," the sterilization of the latter animal is only effected after twelve hours, so that the favourable influence of the "pre-critical period" has disappeared. The more probable hypothesis is as follows:—If the rats treated during the "pre-critical period" are cured more rapidly it is because during this period the organism has undergone a preparation which renders it able to destroy the spirochaetes both easily and promptly. By the administration of the drug at this opportune moment one causes a precocious crisis and the organism combats the infection with its usual forces, phagocytosis and possibly spirochaeticidal substances developed in the blood.

The importance of these results cannot be over-estimated, for they show that there is an opportune moment for the administration of "606" in the treatment of spirochaetal diseases. In the case of relapsing fevers the opportune moment is during the pre-critical period. It remains to be seen whether one can find a similar period in the case of syphilis.

[In the short space at the reviewer's disposal it is impossible to do justice to this excellent article, which is accompanied by curves and tables that clearly support the theories advanced.]

E. H.

Cultivation.

Noguchi (Hideyo). **The Pure Cultivation of** *Spirochaeta duttoni*, *Spirochaeta kochi*, *Spirochaeta obermeieri*, **and** *Spirochaeta novyi*. —*Jl. Exper. Med.* 1912. Aug. 1. Vol. 16. No. 2. pp. 199–210. With 2 plates.

Noguchi, by a similar method to that employed by him in the cultivation of *T. pallidum*, has succeeded in the culture of these four varieties of blood spirochaetes. The following method was found to be the most satisfactory:—Into a sterile test-tube place a piece of fresh tissue—usually rabbit-kidney. Add a few drops of citrated blood from the heart of the infected mouse or rat, and quickly pour about 15 cc. of sterile ascitic or hydrocele fluid into the tube. The contents of some of the tubes are covered with a layer of sterile paraffin oil, while others are left without oil. Incubate at 37° C.

It is advisable to employ the infected blood of a rat 48-72 hrs. after inoculation and before the spirochaetes have reached their maximum multiplication. With this method the author has succeeded in passing a culture of *S. kochi* through 29 tubes over a period of six months.

To make a subculture, 0·5 cc. of the original culture is added instead of the infected blood as above, but it is also advantageous to add a small quantity of normal rat or human blood.

(1) *Spirochaeta duttoni*.—In this spirochaete the maximum multiplication occurs on the 8-9th day. On the 10th the parasites begin to disintegrate and disappear, and by the 15th day it is exceptional to find any spirochaetes present. Subcultures can be made between the 4th and 9th days. These spirochaetes had not diminished in virulence at the 9th passage.

(2) *S. kochi.*—This variety attains its maximum development in the cultures on the 9th day. Its virulence seemed to diminish, for after the 10th passage it no longer killed rats and mice, and the incubation period was prolonged.

(3) *S. obermeieri* attains its maximum growth on the 7th day.

(4) *S. novyi* is more difficult to grow than any of the preceding varieties. It also attains its maximum growth on the 7th day.

In each case Noguchi examined the living spirochaetes from the cultures with the aid of dark ground illumination. Longitudinal division is stated to have been observed in every case, spirochaetes of all lengths dividing in this manner. Transverse division is said to be extremely rare, if present at all. When the spirochaetes first appear in the cultures numerous short forms are observed, but later all the parasites attain the normal length. Spirochaetes grown under a layer of oil are slightly thinner than those grown without this layer.

[Noguchi's results are of considerable interest, but his observations on the division of spirochaetes need confirmation; it is doubtful whether these parasites multiply by any other method than transverse division preceded by incurvation. It is to be regretted that the author should have employed the specific names *S. kochi* and *S. obermeieri* instead of *S. rossii* Nuttall (1905) and *S. recurrentis* Lebert (1874), respectively, as the latter have priority.]

E. H.

Noguchi (Hideyo). **Reinzüchtung der Spirochäten des europäischen, des amerikanischen und des afrikanischen Rückfallfiebers.**—*Münchener Med. Wochenschr.* 1912. Sept. 3. Vol. 59. No. 36. pp. 1937–1938.

Contains a preliminary account of the manner in which the author was able to cultivate various species of blood spirochaetes (see above). In addition, the culture of *S. gallinarum* is described. This was effected in exactly the same manner as that of the human blood spirochaetes; up to date there had been eight passages.

E. H.

Other Papers.

Nicolle (C.) et Blaizot (L.). **Nouveaux Points de l'Etude Expérimentale du Spirochète de la Fièvre Récurrente Nord Africaine. Réceptivité du Lapin.**—*Bull. Soc. Path. Exot.* 1912. July. Vol. 5. No. 7. pp. 472–476.

By the intravenous injections of large quantities of infected blood the authors were able to maintain the spirochaete of a Tripolitan strain of relapsing fever through 12 rabbits in succession, without any diminution in virulence. Uhlenhuth and Haendel found this animal to be quite refractory to strains of African, American, and European relapsing fevers, respectively; yet by the injection of sufficient quantities of blood the least pathogenic of the "*recurrentis*" group of spirochaetes has been shown to be capable of infecting it.

The authors proceed to consider the means of distinguishing the different strains of spirochaetes. Of the three methods employed, the receptivity of laboratory animals has been shewn to be uncertain, cross immunisation is even more so, and at present the only criterion is the agglutination test.

E. H.

FRÄNKEL (Leonid). **Zur Biologie der Rekurrensfäden.**—*Virchows Arch. f. path. Anat. u. Physiol.* 1912. July 18. Vol. 209. No. 1. pp. 97–125. With 45 text figures.

After the examination of 150 cases of relapsing fever in Russia, the author believes that he has obtained proof that the spirochaetes attack both the leucocytes and the red blood corpuscles. The spirochaete is said to invade the leucocytes and cause degenerative phenomena in them, such as vacuolisation of the cytoplasm and breaking up of the chromatin of the nucleus. Phagocytosis, in the sense of the leucocytes taking in and digesting living and virulent spirochaetes, is therefore strongly denied. The paper is illustrated by 45 photo-micrographs of appearances in support of the author's hypotheses.

In addition Fränkel fed 3 *Stomoxys calcitrans* on a patient infected with relapsing fever and subsequently on a man and a woman, without producing any infection. Nevertheless the spirochaetes were found to preserve their form in the gut of the fly for some hours.

[The theories advanced in this long paper are not supported by the author's figures, which represent appearances indistinguishable from artefacts.]

E. H.

FONTANA (Arturo). **Metodo per Colorare Intensamente e Rapidamente il *Treponema Pallidum* ed altri Spirocheti.** [A Method for the Rapid and Intense Colouration of *Treponema pallidum* and other Spirochaetes.]—*Pathologica.* 1912. Oct. 1. Vol. 4. No. 94. pp. 582–583.

Dilute the material to be examined in a drop of distilled water, spread out over a slide, allow to dry in the air, and then fix in the flame. On to the slide pour a few drops of a five per cent. solution of tannic acid in distilled water, and heat gently for about twenty seconds; then wash in running water for thirty seconds. Now add a few drops of an ammoniacal solution of silver nitrate (prepared by adding ammonia to a five per cent. solution of $Ag\ NO_3$ in distilled water until the precipitate at first formed is just redissolved, giving a faintly opalescent solution) and warm the slide for twenty to thirty seconds according to the degree of coloration required. Then wash in water and dry between filter paper. The whole process occupies about seventy to eighty seconds. The spirochaetes are coloured either an intense yellow or brown and, as shown by the author's photographs, are very conspicuous. This method has given good results in the case of *T. pallidum*, *Spirochaeta refringens*, *S. balanitidis*, *S. dentium*, and *S. buccalis* respectively.

[The simplicity of this method of colouration together with its rapidity should make it most useful for diagnostic purposes.]

E. H.

SLEEPING SICKNESS.*

Transmission.

Kinghorn (Allan) and Yorke (Warrington). **On the Influence of Meteorological Conditions on the Development of *Trypanosoma rhodesiense* in *Glossina morsitans*.—*Brit. Med. Jl.* 1912. Oct. 5. pp. 835–837; also in *Ann. Trop. Med. & Parasit.* 1912. Oct. 18. Vol. 6. No. 3. B. pp. 405–413. With Addendum.

Since the Luangwa Sleeping Sickness Commission has had its quarters on the Congo-Zambesi watershed evidence has accumulated which indicates that meteorological conditions have a very pronounced influence on the development of *T. rhodesiense* in *Glossina morsitans*. At Nawalia (circ. 2,100 ft.) in the valley eight transmission experiments were made; at Ngoa on the plateau (circ. 4,400 ft.) five. The results are shown in two tables. It is seen that at Nawalia the mean temperature in the eight experiments lay between 75° and 83°, the absolute maximum varying from 85° to 93° and the absolute minimum from 60° to 74°. On the plateau the mean temperature lay between 59° and 62°, the absolute maximum between 72° and 74°, the absolute minimum between 42° and 50°. Of 330 flies used in the valley six, and probably ten, became infective, the larger figure being based on the number of salivary gland infections. In the five plateau experiments 520 flies were employed, without one becoming infective. The most striking difference in the conditions under which these experiments were performed was in the temperature: roughly speaking this was 15° to 20° higher in the valley than on the plateau.

In a further series of experiments made on the plateau the flies were kept in an incubator at a temperature approximating to that in the valley; 61 were used in one experiment, 72 in another. Though the majority of the flies had died in seven days, one infective fly at least was obtained in each experiment. It is noted that infective wild flies were met with on the plateau during the period of the unsuccessful laboratory experiments; it is suggested that these flies were infected during the warmer season and had survived into the cold season. The results of feeding freshly-caught flies on healthy monkeys in the valley and on the plateau respectively are compared. In the valley 3,202 flies were fed in 29 batches and *T. rhodesiense* was isolated in six instances, giving a ratio of infective to non-infective of 1:534. On the plateau 5,041 flies were fed in groups on 39 monkeys, with four positive results, 1:1,260. As tsetse flies and game are about equally numerous at the two places and these are less than seventy miles apart, the authors think that the only essential difference is in the climatic conditions.

They note that at the most favourable season of the year for transmission experiments in the valley and also in the case of those carried out in the incubator the relative humidity was extremely low; they cannot say at present whether this is more than coincidence.

In the Addendum is published an experiment which shows that flies fed on an infected animal on the plateau and non-infective

* This section forms a continuation of the *Sleeping Sickness Bulletin*, the last number of which was published in September.

after forty days became infective eight days or less after being placed in an incubator, whereas the control flies did not. It is suggested that the first part of the cycle can take place at a comparatively low temperature, but that a higher temperature is needed for its completion.

The authors' summary is as follows:—

"The developmental cycle of *Trypanosoma rhodesiense* in *Glossina morsitans* is, to a marked degree, influenced by the temperature to which the flies are subjected. High temperatures (75-85° F.) favour the development of the parasite, whilst low temperatures (60-70° F.) are unfavourable."

A. G. B.

ROBERTSON (Muriel). **Notes on the Polymorphism of *Trypanosoma gambiense* in the Blood and its Relation to the Exogenous Cycle in *Glossina palpalis*.**—*Proc. Roy. Soc.* 1912. Oct. 11. Series B. Vol. 85. No. B 582. pp. 527–539.

General condition of a T. gambiense *infection.*—It is noted that a close study of any given infection brings out very clearly that the multiplication of the trypanosomes occurs in the circulating blood. Search has been made for any type of multiplication in the cells of the lung, liver, and spleen, but so far without success. The author thinks that the invariable correlation between a rise in the number of trypanosomes and a rise in the percentage of dividing forms makes such a development very improbable. The factors controlling the number of flagellates present in the blood at a given time are discussed. The author's work has been done with monkeys.

The drop in the number of trypanosomes is often sudden, but the completeness of the clearance varies within wide limits, and the duration of the depressed period is quite inconstant. The mechanism by which the trypanosomes are destroyed has not been studied; the work of other observers points to phagocytosis, or lysis in the blood stream. All the evidence is against the possibility that the trypanosomes enter the host's cells; after their absence they reappear relatively gradually and their appearance is always accompanied by active multiplication in the blood stream. The coming and going of the trypanosomes is called the endogenous cycle.

Method.—Blood films were taken daily from a *gambiense* monkey at the same hour, dried in the air, and stained with Giemsa. They were measured by means of a compass set at one micron distance, as in BRUCE's method. The criticisms of Dr. STEPHENS are considered (see *Sleeping Sickness Bulletin* Vol. 4, p. 145). It is remarked that the projection of the trypanosomes on to a screen is at present impossible in Central Africa; moreover, slight inaccuracy is not material because it is the relative and not the absolute lengths that are significant. Cages of newly-hatched flies were fed daily on selected monkeys and the number of flies infected were ascertained.

The endogenous cycle.—There is really no sharp distinction of the trypanosomes into separate types, but rather a continued transition from one type to another. After a discussion of the forms seen at different periods in the cycle this is interpreted as follows—

"The short forms (15-20 μ) constitute the normal adult blood type; this expression is merely used to indicate the form which has the largest duration

in time in the cycle and which is the most stable. These increase in size and bulk, and form that sliding scale of individuals which may be termed the intermediate forms; these in turn lengthen out to the long, more slender types, which proceed to divide, giving rise once more to the short forms."

The sex interpretation appears to the author so improbable as hardly to merit discussion.

The Relation of the Endogenous Cycle to the Production of the Infected Fly.—The author tried to find out whether any definite condition either of the individual parasite or of the infection as a whole was requisite for the production of infected Glossina. The observation on negative periods in monkeys was confirmed (see *Sleeping Sickness Bulletin* Vol. 4, p. 267). It is noted that positive results are obtained in spite of a general tendency on the part of the flies to digest their parasites. A transmitting host whose digestion is rapid tends to have a relatively low percentage of carriers: thus, mosquitoes, fleas, and tsetse flies all produce relatively few carriers; whereas leeches and ticks, whose digestion is very slow, give ninety to a hundred per cent. Immediately after a drop in numbers there are very few trypanosomes and all are of the short type. This is an effective period and generally produces about the average number of *plus* flies. The trypanosome population has just suffered a process of elimination; these trypanosomes are therefore the resistant ones, as well as those capable of producing infection in flies. These results again are opposed to a sex interpretation of the dimorphism.

The general summary is as follows—

"1. *T. gambiense* is a polymorphic species with a continuous range of variation.

"2. The shorter forms of 14-20μ in length constitute the normal adult blood type.

"3. The intermediate individuals measuring 20-24μ in length are growth forms and lead to the long forms of 23-33μ, which are those about to divide. The polymorphism of the trypanosome is thus due to growth and division phenomena and does not correspond to a sex differentiation.

"4. The shorter forms are those destined to carry on the cycle in the transmitting host.

"5. There are definite periods when the blood is not infective to fly although trypanosomes are present. Such periods are (*a*) just before an outburst of multiplication; (*b*) during the destruction of trypanosomes preceding a depressed period; (*c*) the summit of an exalted period involving very numerous trypanosomes—at such a time the parasites very frequently show signs of exhaustion; (*d*) certain periods of rapid multiplication when both the absolute and relative numbers of the shorter forms are low."

A. G. B.

DUKE (H. L.). Some Observations on *Trypanosoma pecorum* (Bruce) and *T. uniforme* (Bruce).—*Proc. Roy. Soc.* 1912. Oct. 11. Series B. Vol. 85. No. B 582. pp. 554–561.

T. pecorum.—Though this trypanosome seems to be widely distributed in Uganda nothing definite is known concerning its true carrier in nature; *G. palpalis* would appear to be at most a facultative host. Again, nothing is known of its natural reservoir. Experiments were undertaken to discover whether *T. pecorum* is pathogenic to antelope or whether this animal is able to act as a reservoir. A young bushbuck born in the laboratory was inoculated from a monkey; trypanosomes appeared in its blood fifteen days later. At intervals clean flies were fed upon this bushbuck and afterwards upon clean monkeys. Flies

dissected three months later were found to contain flagellates. There was one doubtful instance of transmission to a monkey; the fly (No. 9) which was probably responsible had its sucking stomach swarming with trypanosomes. A table is given showing the distribution of flagellates in fifteen infected flies dissected between the ninth and the 141st day. It is seen that only fly No. 9 had an infection of the sucking stomach. In every case the hind-gut was infected. No infection of the proboscis was observed before the 76th day; afterwards it was present in four cases out of five. The salivary glands were examined in three cases with negative result. Later, the blood of the bushbuck was injected into animals. A calf was thus infected 323 days after the original infection of the bushbuck. The bushbuck was throughout in good health.

T. uniforme.—According to Bruce and his collaborators this trypanosome causes a fatal disease in domestic ruminants. In Duke's experience *T. uniforme* is not a fatal trypanosome; in only one instance has an animal died of the infection. Two situtunga brought alive to the laboratory were found to harbour this trypanosome as a natural infection. Laboratory-bred *G. palpalis* were fed on them from time to time. It was shown that the animals were still capable of infecting these flies after a period of ten months; trypanosomes were found in the proboscis only.

The author notes that in Uganda alone *T. gambiense, T. vivax, T. pecorum* and *T. uniforme* have all been proved capable of surviving for a considerable time in antelope, apparently without exerting any injurious effect upon them.

A. G. B.

Sleeping Sickness Investigations in Uganda.

Reports of the Sleeping Sickness Commission of the Royal Society, No. 12. 1912. London: H.M. Stationery Office. 145 pp. and 30 plates. Price 5*s.* 6*d.*

This volume contains sixteen articles, of which nine have been published in full and two in part in the *Proceedings of the Royal Society.* These have been summarised in the *Sleeping Sickness Bulletin.* There remain five papers, all on work done in Uganda.

i. *The Development of Trypanosomes in* Glossina palpalis (Fraser and Duke, pp. 36-56)—

All the flies used in these experiments were hatched in the laboratory from pupae collected on the shore of the Victoria Lake. A table is given of the laboratory temperatures during the eight months they lasted.

T. gambiense.—Seven experiments were done to transmit *Trypanosoma gambiense* by *Glossina palpalis.* The infected animals were in each case monkeys. The data, in some experiments imperfect, are given in a table. The number of days the flies were fed on an infected animal was two in four instances and one in three. In one case only was transmission effected. Several of the experiments are given in detail. A table gives the result of the fly dissections. Of 384 flies dissected at various periods between the first and the eightieth day 32 were positive, all examined between the first and the thirtieth day, but it is noted that in the one successful experiment the flies remaining on the

62nd day were the only ones dissected. In all the positive flies the gut, especially the midgut, was the chief site of infection with flagellates; in the majority the proventriculus was negative. Flagellates were seen a few times in the salivary glands, never in the proboscis. Three plates illustrate the morphology of the forms seen, another that of a remarkable flagellate, which is evidently *T. gallinarum* (see *Sleeping Sickness Bulletin* Vol. 4, p. 351).

Similar experiments were done with *T. brucei*, *T. pecorum* and *T. uniforme*; their morphology in the flies is shown in a series of plates. The conclusions are as follows.—

"*Trypanosoma gambiense, brucei, pecorum,* and *uniforme* undergo a development in laboratory-bred *Glossina palpalis.*

"2. In the case of *Trypanosoma gambiense* and *brucei* the gut is the chief site of development.

"3. In *Trypanosoma pecorum* the proboscis in addition to the gut is usually infected after the 50th day from the infected feed.

"4. Development of *Trypanosoma uniforme* in the fly is limited to the proboscis."

ii. *The Duration of the Infectivity of the* Glossina palpalis *after the removal of the Lake-shore population* (Fraser and Duke, pp. 63-75)—

This was a continuation of the work of the Sleeping Sickness Commission of the Royal Society 1908-9. The experiments are given in detail, their object being to ascertain if wild *G. palpalis* were capable of giving rise to Sleeping Sickness in healthy monkeys. The following table shows the results—

Table I.

Date.	Experiment.	Place.	No. of flies put on.	Result.	Remarks.
1910.					
Aug. 8–15	21	Kibanga	44	+	Flies caught on mainland.
„ 16–Oct. 19 ...	48	„	3,220	—	
Sept. 1–Dec. 31 ...	122	„	6,625	—	
„ 25–Oct. 1 ...	198	Nsanga	2,390	—	
„ 28–Oct. 1 ...	199	„	1,940	—	
Oct. 2–6	208	„	2,090	—	
„ „	209	„	1,780	+	
„ 7–13	223	„	2,160	+	
„ „	224	„	2,580	—	
„ 22–Nov. 7 ...	289	Bukafu	1,750	—	
„ „ ...	290	„	1,750	—	
Nov. 16–21	321	Kibanga	850	+	
1911.					
Jan. 3–Feb. 22 ...	478	„	6,279	—	
Feb. 13–20	597	„	3,075	+	
„ 23–Mar. 16 ...	633	„	6,095	—	
„ 27–Mar. 31 ...	641	„	8,450	—	
Jan. 22–29	557	Kimi Island	4,324	—	Flies caught on islands.
„ „	558	„	4,120	—	
Feb. 2–10	591	Nsadzi Island	3,265	—	
„ 4–10	592	„	2,500	—	

"When these results are compared with those reported by the Sleeping Sickness Commission of the Royal Society, 1908-09, the point which is most

striking is the large number of negative experiments now recorded and the great increase in the number of flies necessary to infect a healthy monkey with *Trypanosoma gambiense* by feeding wild *Glossina palpalis* upon it. When the 1908-9 Commission's experiments were carried out—from November, 1908, until September, 1909—about 500 flies caught on the mainland were usually sufficient to infect a monkey. We now find from observations made during the period August, 1910, to March, 1911, that some 10,000 are required, and that during the latter half of that time 28,294 flies were put upon susceptible monkeys, and caused only one infection. These facts seem to indicate that the infectivity of Lake-shore *Glossina palpalis* is gradually becoming less.

"There are, however, still a few infected flies to be found. Where they derive their infectivity it is impossible to say definitely."

It is noted that a few natives, some of them islanders, still remain on the Lake shore and it does not seem unlikely that they may be the source of infection. In any case, *G. palpalis* on the Lake shore have been shown capable of infecting monkeys with *T. gambiense* three years after the removal of the population.

iii. *Various Experiments* (Fraser and Duke, pp. 75-78)—

These include experiments on hereditary transmission, on the longevity of laboratory bred *Glossina palpalis*, and the possibility of *G. palpalis* acquiring *T. grayi* by contaminated feeding. In the experiments to test the longevity of the flies 260 were fed daily till their natural death. One female survived till the 185th day; the others died at earlier periods, two being still alive after 160 days.

iv. *Experiments devised and carried out by Dr.* van Someren (pp. 78 and 79)—

Five *T. gambiense*-infected monkeys were treated by arsenophenylglycin. According to the table the dose was 0·5 gm.; according to the text 5 gm. One animal survived 178 days; the others died between the third and 41st day. Two experiments to see if *Stomoxys* can act as a carrier of trypanosomes were negative. Apparently, few flies were alive when the flies were transferred to the healthy monkey.

v. *Progress Report on Investigations into the Bionomics of* Glossina palpalis, *July* 27, 1910, *to August* 5, 1911 (G. D. H. Carpenter, *vide infra*).

A. G. B.

Bionomics of Tsetse Flies.

Carpenter (G. D. H.). **Progress Report on Investigations into the Bionomics of *Glossina palpalis*, July 27, 1910, to August 5, 1911.**—*Reports of the Sleeping Sickness Commission of the Royal Society.* 1912. No. 12. pp. 79–111. With 4 plates.

These investigations were chiefly concerned with the following points—(1) Length of life of the fly, (2) Duration of infectivity of the Lake shore fly, (3) Natural enemies, (4) Breeding grounds, (5) Food supply. An account is given of the places selected for work; one was on the mainland and two were islands.

The method adopted to ascertain the length of life of the fly was to mark large numbers by amputation of the leg through the centre of either the tibia or fibula and to ascertain how long afterwards marked specimens could be caught at the same spot.

Between July 27 and October 15, 1910, 8,143 were so marked and liberated, females slightly predominating. Marked flies subsequently caught were noted and liberated. The results are shown in a table. The search for marked flies was continued up to February 11, 1911. After the end of January *G. palpalis* had become much reduced in numbers, so that few could be caught. One female fly was retaken 182 days after it was marked; it was probably then a freshly hatched fly. A male fly retaken had a minimum life duration of 149 days. [Compare the results of FRASER and DUKE above.] The relation between the meteorological conditions and the number of flies caught is shown in a chart. It is noted that a decrease in the relative humidity of the atmosphere is responsible for a large drop in the number of flies; they are killed off in large numbers at the onset of the dry weather.

Duration of Infectivity.—On Damba Island a monkey showed trypanosomes after it had been fed on by 885 flies. The last inhabitant had been removed from the island a year and ten months previously.

Natural enemies (a) *of the pupa.*—No evidence was obtained that these are destroyed by vertebrates. No parasites were bred from 5,600 pupae kept in wooden boxes. Of the pupae found in nature, some had a small round hole indicating the exit of a parasite, and others a larger irregular opening made from outside by an enemy which devoured the contents. Carpenter was unable to discover what insect made this hole.

(b) *of the perfect fly.*—He examined the stomach contents of 26 bee-eaters and 26 other birds of insectivorous species, all with negative results. The observations of ROUBAUD* on the fossorial wasp *Bembex* as an enemy of tsetse flies were confirmed and extended. The burrows are constructed in light soil or sand. Carpenter remained near a burrow and watched a *Bembex* catch *palpalis* off his clothes. It caught thus 29 *palpalis* and two other flies in three and a quarter hours. Afterwards he opened up the burrow and found a full-grown larva with 31 tsetse flies; ten were females and of these eight contained large larvae. The *Bembex* has its own enemy, a small Muscid fly of the genus *Idia*, which enters the burrow and lays its eggs there, so that its larvae consume the flies intended for the *Bembex* larvae. Carpenter kept a *Bembex* larva in captivity. In 21 hours it eat nine specimens of *Glossina palpalis*. Unfortunately the *Bembex* does not confine its attentions to tsetse flies, and the ground everywhere is not suitable for its burrows. No evidence was obtained of any disease amongst *Glossina palpalis*.

Breeding grounds.—These are described, with photographs. The place where most pupae were obtained (2,000 to 3,000 monthly) is formed of small pebbles mixed with coarse sand, left owing to subsidence of the Lake some four to five feet above its present level, and about four to five yards from the present water's edge. The belt of vegetation comes to an abrupt end and pupae are found at the edge of this belt, which faces south-east and is in shade after midday. The flies were never seen to deposit their

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* *Compt. Rend. Acad. Sci.* 1910. Vol. 151. No. 8. pp. 505-508.

larvae in the sun; Carpenter witnessed the birth of eight. The conclusions are these—

"1. Favourite sites for depositing pupae are those which are in shade, but where there is free air circulation.

"2. The soil, commonly gravel or coarse sand, must be dry and loose.

"3. The fly does not extrude its larva until the middle of the day, always selecting a shady spot."

Food supply.—An attempt was made to find out why the proportion of the sexes collected differ on the mainland and on the islands. Flies were examined on the mainland and on islands to find out what proportion contain mammalian and non-mammalian blood respectively. No evidence was obtained of a female preference for mammalian blood. The chief source of non-mammalian blood on Damba Island is, Carpenter believes, cormorants and darters or the Varanus lizard. On two occasions he observed numbers of *Glossina palpalis* attacking Varanus, he himself not being touched. He has never seen a tsetse drink water nor insert its proboscis into vegetable tissues. On Damba Island the gut of 455 flies was examined for vegetable organisms. Numerous organisms were found, which are depicted in three plates.

Bacilli and Trypanosomes.—In the examination of 600 flies the frequency of occurrence of bacilli and trypanosomes was noted. The fore part of the gut was sometimes of a bright carmine colour; this was found to be due to a mass of amorphous granules of a translucent carmine colour lying in the lumen, called here carmine granules. The results are given in a table.

Table V.

—	T. Trypanosomes.	B. Bacilli.	G. Granules.
1. Percentage of total flies containing either T., B., or G.	11	19·3	5·5
2. Percentage of each heading, of males ...	43·9	50·8	33·3
3. Percentage of each heading, of females...	56·1	49·2	66·7
4. Percentage of cases under each heading in which T. also occurred.	—	3·4	51·5
5. Percentage of cases in which B. also occurred.	6·1	—	9·1
6. Percentage of cases in which G. also occurred.	30·3	2·6	—

The table shows that it is extremely uncommon to find both bacilli and trypanosomes in the same fly. There would appear to be some connection between the carmine granules and the trypanosomes. The granules are non-crystalline and insoluble in alcohol and water. The conclusion is that there is marked incompatibility between trypanosomes and bacilli in the gut of the fly.

Contents of the gut of freshly-bred flies.—The flies examined had just emerged from the pupae and had the proboscis bent under the thorax. 205 were examined and bacilli were present in 9·8 per cent. In addition there were seen large crystals. Various

organisms also were found in the gut of these bred flies and one in a larva; they are figured. One was believed to be a larval nematode.

The sex proportion.—Of 1,400 flies bred from pupae obtained on Damba Island 48 per cent. were male and 52 per cent. female, whereas in nearly 5,000 caught during the same period 78 per cent. were male and 21 per cent. female. The cause of this is obscure.

Tsetsefuges.—Four preparations were tried and found to be useless.

The vitality of pupae.—Pupae were submerged in water and exposed to the sun. The submersion experiments showed that should any breeding ground be flooded at intervals by heavy rains all the pupae would not be destroyed; even four successive submersions for 24 hours did not destroy more than half. Other experiments showed that complete submersion between 108 and 120 hours is necessary to destroy the pupae totally, and that a certain proportion can survive flotation for eight days. Other experiments showed that, though neither twelve hours' submersion nor fourteen hours' exposure to sun have, alone, any effect, if employed alternately they are fatal. Pupae covered with one inch of earth and repeatedly exposed to the sun all died.

A. G. B.

VORWERK. Bericht über Versuche mit Fliegenleim. [Experiments with Tsetse Lime.]—*Arch. f. Schiffs. u. Trop. Hyg.* 1912. October. Vol. 16. No. 19. pp. 651–658.

These experiments were devised to see if *Glossina palpalis* could be exterminated in circumscribed areas by CLEVE's tsetse lime method. They were carried out at the mouth of the river Mnege (? Tanganyika), where this species is numerous and where four isolated groves of trees stand. Fly communication between these was prevented by the destruction of the long grass and reeds. The experiment took place in March during the rainy season. To begin with, practised fly-catchers caught flies in each of the four places between eight o'clock and midday. Every day for a fortnight a goat provided with limed cloths was taken to each place, tended by a boy provided also with limed cloths. At the end of the fortnight control catches were made by the fly-catchers, and fourteen days later more controls. The results are shown in a table. It is noted that the numbers of flies caught did not steadily diminish, but after a preliminary diminution remained stationary; that a single fly-catcher in four hours caught about the same number of flies as a man-trap and goat-trap together during the whole day; and that at the end of the experiment the number of flies had diminished in each group. However, at the second fly catching, fourteen days later, the numbers had increased again. It is concluded that it is not possible to exterminate *palpalis*, even under favourable conditions and in a small space, by this method. The boy and the goat were free from trypanosomes at the outset; at the end of the experiment each was found to be infected. It is doubted whether

the boy's infection was contracted during the experiment, but it is advised that natives who take part in such demonstrations should be kept under the influence of atoxyl. It is noted that more male flies were caught than female, and more than three times as many on the boy as on the goat. Some details of cost are given. The lime was of no use for catching mosquitoes.

By means of the lime spread on a board four rats were caught by the tails; the rest disappeared from the building. It is suggested that the lime, which has small value in exterminating tsetse flies, may have a future as a rat-trap.

[These results correspond with those of Koch, whose experiments concerned *G. morsitans* in German East Africa (*Sleeping Sickness Bulletin* Vol. 4, p. 263). He demonstrated 'the great superiority of a single fly-catcher over not only a single fly-trap but the whole lot put together.' The lime method may have its uses, but they are more limited than Cleve's experiments seemed to show.]

A. G. B.

Morphology.

Schepilewsky (E.). **Fadenförmige Anhängsel bei den Trypanosomen.** [Thread-like Appendage in Trypanosomes.]—*Centralbl. f. Bakt.* Abt. I., Orig. 1912. July 3. Vol. 65. Nos. 1–3. pp. 79–83. 1 plate.

The author first gives an account of the well-known morphology of *Trypanosoma brucei* and *T. equinum*, and a short review of the work of Wasielewski and Senn, who observed elongation of trypanosomes in slides of rat blood. Wendelstadt and Fellmer also noted elongation and free flagella, as did other workers cited by the author in some detail. The chief interest of the paper lies in Schepilewsky's own observations on *T. brucei* and *T. equiperdum* using Reichert's "*Spiegelkondensor*." With this form of ultra-microscope the flagellum of a trypanosome is seen to be surrounded by a thin pellicle along its whole length, so that, strictly speaking, there is no true free flagellum. In the living *T. brucei* and *T. equiperdum* one can often see thin, thread-like appendages arise either from the apex (*Spitze*) of the flagellum or from the hinder, blunt end of the body or sometimes even from both. The threads resemble spiderwebs, are of even contour, are very refractile, and vary in length, some being $1\frac{1}{2}$ to 2 times the length of the body. When a thread arises at the posterior end the appearance of a *Trypanoplasma* is produced. The origin of the threads is undoubtedly from the flagellum. When the trypanosomes move the threads often drop off. At the death of the trypanosome the threads dwindle rapidly, break up into granules and are dissolved.

The author appears to suggest that the loss of the threads disturbs the stability of the trypanosome, and makes one conjecture whether the threads may be of protoplasmic origin.

H. B. Fanthan.

BLACKLOCK (B). **On the Presence of Posterior Nucleated Parasites in a Strain of *T. brucei*.—*Brit. Med. Jl.*** 1912. Oct. 19. p. 1057.

The strain in question came from Uganda and was obtained from BRUCE in September, 1910. It having been observed during other experiments that some of the short stumpy forms had the nucleus posterior to the centre, films taken from the laboratory animals at the Runcorn Laboratories were carefully examined. It was found that in films from rats, rabbits, and guinea-pigs such forms appear, usually in small numbers. These are figured. In no case was the nucleus seen to lie posterior to the blepharoplast, but in some it approached it closely.

[Since the posterior nucleated forms in *T. rhodesiense* were described, similar forms have been found by WENYON in '*T. pecaudi*' (? *brucei*) from the Sudan, by YORKE and BLACKLOCK in *T. equiperdum* (laboratory strain) and now by BLACKLOCK in *T. brucei* (Uganda).]

A. G. B.

CULTIVATION.

THOMSON (John Gordon) and SINTON (John Alexander). **The Morphology of *Trypanosoma gambiense* and *Trypanosoma rhodesiense* in Cultures: and a Comparison with the Developmental Forms described in *Glossina palpalis*.—*Ann. Trop. Med. & Parasit.*** 1912. Oct. 18. Vol. 6. No. 3. B. pp. 331–356. With 3 plates.

Many culture media were tried by the authors; the most successful were the following:—

(1) A modified Novy-MacNeal-Nicolle medium, made by substituting citrated rat's blood for defibrinated rabbit's blood. The medium consists of agar 14 grammes, pure sodium chloride 6 grammes, and distilled water 900 c.c. The agar must be carefully washed and the medium sterilised at 100° C. for 20 minutes on three successive days. To this a sterile mixture of rat's blood (from the heart) and sodium citrate (1 per cent.) is added. The mixture consists of about two parts rat's blood to one part citrate.

Equal quantities of the agar medium and citrated blood were used. The tubes were kept in a water bath at a temperature of 45° C. for half an hour, to destroy the complement without making any appreciable change in the character of the blood. They were incubated for two days at 25° C. to allow the water of condensation to collect. Such a medium was found most suitable for the culture of *Trypanosoma gambiense* and *Trypanosoma rhodesiense*. Citrated human blood, treated similarly, was also useful.

(2) A fluid medium also was tried successfully. It consisted of human pleuritic fluid (rendered complement free by heating to 45° C. for one hour), to which was added one-third its volume of citrated human blood.

All the media, however, are somewhat uncertain.

The blood used to inoculate tubes was obtained, aseptically, from the heart of an infected rat just killed. The cultures were incubated at 22° C. to 24° C.

The authors' summary and conclusions are as follows:—

(1) *T. gambiense* and *T. rhodesiense* are capable of being cultivated on artificial media. *T. gambiense* has been cultivated for a period of thirty-seven days, and during that time was carried through four generations by means of sub-cultures. *T. rhodesiense* has been more difficult to cultivate and has continued to develop for only twenty-one days. All the flagellates disappeared in the third sub-cultures.

(2) The life history of these trypanosomes in culture tubes is similar to that which occurs in the gut of the insect host. This is shown by a comparison of the morphological characters of *T. gambiense* in cultures with those forms found by Sir David Bruce and his colleagues in *Glossina palpalis.* We find that the developmental forms found in the culture tubes are identical in their chief characteristics with those described by Bruce in the gut of an infected tsetse-fly.

(3) The cultures of *T. gambiense* and *T. rhodesiense* quickly lose their infectivity, and intraperitoneal injections of these into rats after the third day have been unsuccessful in causing an infection. This we have shown to be comparable to the results of Sir David Bruce and his colleagues, who have found that the intestinal contents of *G. palpalis* quickly become non-infective. The infectivity during the first few days appears to be due to the persistence of some of the original blood forms. In successful cultures, therefore, we expect infectivity to cease as soon as these blood forms disappear and the 'healthy developing forms' which have been shown by Bruce to be non-infective appear.

(4) Our cultures of *T. gambiense* and *T. rhodesiense* have remained non-infective after the third day, and we believe that this is explained by the fact that the infective [short, stumpy] forms such as found by Bruce and his colleagues in the salivary glands of *Glossina palpalis* did not occur in our cultures, and we have suggested that probably some transference of the cultures to a new medium or environment similar to that of the salivary glands of the tsetse-fly might be required to permit the full life history of the trypanosomes being completed.

(5) Cultures of *T. rhodesiense* seem to differ from those of *T. gambiense.* In cultures of the former typical posterior nuclear forms such as described by Stephens and Fantham (1910) are relatively common, whereas in the latter they are of very rare occurrence.

(6) Although the so-called 'male' and 'female' forms are present in cultures we were unable to find any definite evidence of a sexual cycle.

The paper is well illustrated. There is a coloured plate showing the cultural forms of *T. gambiense* and a similar one of *T. rhodesiense.* There is a third plate of microphotographs of a division rosette and a colony of *T. rhodesiense.*

H. B. F.

Sleeping Sickness News.

Nyasaland and Rhodesia.

In Part 17 of the *Sleeping Sickness Diary,* by Dr. H. Hearsey, P.M.O., dated June 30th, 1912, it is stated that thirteen cases of sleeping sickness had been notified in Nyasaland during the last quarter. These added to the 63 previously reported make a total of 76. Twelve of these cases were discovered by Dr. Shircore, now in charge of the sleeping sickness area. An account of each case is given. Three medical officers who had been investigating in the adjoining districts had not, at the time of writing, been successful in finding cases; it is considered probable, however, that these exist. An account is given of a case of trypanosomiasis in a European contracted in Portuguese East Africa, recorded by Dr. Stannus (see *Sleeping Sickness Bulletin*

Vol. 4, p. 266). A second case of trypanosomias is from Portuguese East Africa, in a native, has been recorded. An account is given of the administrative measures taken to restrict the disease.

Dr. A. May, P.M.O., Northern Rhodesia, says that up to the end of June 1912 seventy cases of trypanosomiasis had been found in that country. It is thought that a greater number has escaped observation. Almost all the cases have come from the Luangwa closed area; with the exception of four natives still under treatment all have ended fatally.

A. G. B.

*French Congo.**

The investigations of Aubert in the Upper Sangha region (noted in *Sleeping Sickness Bulletin* Vol 4, p. 84) are referred to. The author's visit was paid five months later. At Carnot Aubert found a severe epidemic of sleeping sickness, twenty per cent. of the population being infected. He gave to each patient an injection of atoxyl. The author first examined as many as possible of 253 patients treated by Aubert. 24 had died and no information could be obtained about 81. He examined the blood and glands of 148, and found parasites in the gland juice of seventeen and in the blood of four. In the case of 69 others the blood was centrifuged and trypanosomes were thus found in nine. The author calculates that if all had submitted to this process sixteen relapses would have been thus detected. The total result was that five to six months after a single injection of atoxyl 25 per cent. of the cases had relapsed, a result which is characterised as satisfactory. [It is not stated here nor in Aubert's paper what dose of the drug was given.] The details are given in tables.

The author looked for fresh cases at Carnot. The diagnosis was made by examination of gland juice and direct examination of the blood. The result showed that 26 per cent. of the natives were infected and a still higher percentage in the surrounding villages. Tables again are given.

He notes that his observations generally agree with those of Aubert, both as to the incidence of the disease and the presence of *Glossina palpalis*. At Carnot this fly was very rare; during his stay he saw only one specimen. The plateau on which the town is built has been completely cleared and many of the villages have been moved. Nevertheless, the epidemic continues to spread. The immediate result of the injections of atoxyl given by Aubert was that the mortality almost completely disappeared, but the improvement lasted only a short time. Montfort draws the obvious conclusion that the treatment must be continued longer. He says that in the neighbourhood of Carnot

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* Montfort. Contribution à l'Étude de la Répartition et de la Prophylaxie de la Trypanosomiase humaine dans la Haute Sangha (Avril–Mai 1911).—*Ann. d'Hyg. et Méd. Colon.* 1912. July–Aug.–Sept. vol. 15. No. 3. pp. 593–612.

horse flies and Stomoxys are numerous and suggests that these may be responsible for the spread. The paper contains a map.

A. G. B.

Belgian Congo.

SCHWETZ (J.). **Les Glossines dans la Vallée de la Lukuga (Tanganyika).**—*Revue Zoologique Africaine.* 1912. September. Vol. 2. No. 1. pp. 49–62. With 1 map.

The Lukuga river, as is shown on a chart, leaves Lake Tanganyika and flows westwards to join the Lualaba river. The observations detailed in this paper were made in the upper third of the Lukuga valley over a distance of 85 kilometres. *G. palpalis* is found without interruption between the Lake and the Lualaba river, and this is of special importance because the valley will eventually be occupied by a railway. The valley is extremely rich in big game and here *G. morsitans* abounds. The spheres of these two species are said to be distinct, *morsitans* not being met with till the observer is many metres from the river bank. *Morsitans* was found not only near, but also in villages. In one spot *Glossina fusca* was numerous. The author says that, generally speaking, it is beyond doubt that sleeping sickness is found only in *palpalis*, not in *morsitans* regions. An account is given of the other rivers on the west side of Tanganyika. At one place a specimen of *G. brevipalpis* was taken, and identified by AUSTEN. On the map which accompanied the paper the distribution of *G. morsitans*, *G. palpalis* and *G. fusca* is shown.

A. G. B.

MISCELLANEOUS.

HALBERSTAEDTER (L.). **Versuche mit einem spontan arsenfesten Trypanosomenstamm.** [Experiments with a Strain of Trypanosomes Spontaneously Arsenic-fast.]—*Arch. f. Schiffs. u. Trop. Hyg.* 1912. October. Vol. 16. No. 19. pp. 641–647.

The author notes that the various species of trypanosomes behave very differently towards individual chemical substances. For instance, trypanred is very effective in mal de caderas, but useless, or nearly so, in nagana; nagana trypanosomes are, therefore, naturally resistant to trypanred. Similarly, there are differences in sensibility to arsenic amongst nearly related spirochaetes and amongst malarial parasites. Moreover, different strains of the same species of trypanosome, propagated in laboratories in small animals, behave in this respect in very different ways; the different behaviour of such strains to arsenicals caused EHRLICH to introduce the terms 'tenax' and 'debilis.' Hitherto, however, a strain spontaneously fast towards the most active arsenicals, such as arsacetin and salvarsan, has not been described.

The strain of which this paper treats was one of mal de caderas obtained by Professor LUTZ from an infected horse in Brazil. Since April, 1908, it had gone through 720 passages in mice or rats. Neither the horse nor any of these animals had been

treated with arsenicals. At the beginning of 1912 it was discovered by chance that the strain was fast to atoxyl; it was therefore tested with other chemotherapeutic agents. It was found to be absolutely fast towards arsacetin and salvarsan; the largest doses which could be given did not influence the course of the infection. Unfortunately, the author had no other strain of caderas with which to compare it, so that one of nagana had to be used for this purpose. The behaviour of the strain was then tested with arsenophenylglycin and it was found that a single injection of 1:600 solution brought about permanent cure. The effect of arsenophenylglycin was tested at the same time on three strains of nagana, one of which was fast to arsacetin. All reacted to arsenophenylglycin. The fact that arsenophenylglycin acts on arsenic-fast strains is explained by EHRLICH by the assumed existence of an aceticoceptor in the trypanosomes, with which the acetic acid radicle of the arsenophylglycin first unites. The strain behaved normally to para-rosanilin-chloral-hydrate (parafuchsin). The action of potassium antimonyl tartrate was then tested; this was of interest on account of the close relation between antimony and arsenic preparations; the strain was found to be easily influenced by this drug, just as was the normal nagana strain.

Lastly, experiments were made on the direct action of salvarsan on trypanosomes in the test tube.

A. G. B.

BORCHERS (Carl). **Einige Beobachtungen über den Wundverlauf bei Schlafkranken. Intravenöse Äthernarkose bei einem Schlafkranken.** [Observations on the Course of Wounds in Sleeping Sickness.]—*Arch. f. Schiffs. u. Trop. Hyg.* 1912. October. Vol. 16. No. 19. pp. 648–651.

The author in the Belgian Congo had occasion to operate on four natives infected with trypanosomiasis. The operations were, a radical cure of hernia, suture of a large contused wound, the removal of adenoids, and the opening of an abscess over the mastoid process. Three of the patients had been previously treated with atoxyl, eight or more half-gram injections, but in one of these trypanosomes were present in the glands. The fourth was a native boy who had a passport allowing him to travel on the railway; trypanosomes were found in his cervical glands. The wound edges in the first two cases had a peculiar bacon-like appearance and abundant thin pus was secreted; the removal of the adenoids was followed by middle-ear suppuration, and in the last case the tissues became gangrenous. All improved rapidly when atoxyl was given. It is noted that in these cases the tissues had been unable to protect themselves against infection, and there was no tendency to heal until specific treatment was instituted.

To the patient operated on for hernia ether was given intravenously by BURKHART's method. Gland puncture done five hours later showed numerous unaltered trypanosomes.

A. G. B.

DELANÖE (M. et Mme. Pierre). **Sur les Rapports des Kystes de Carini du Poumon des Rats avec le *Trypanosoma lewisi*.**—*Compt. Rend. Acad. Sci.* 1912. Oct. 7. Vol. 155. No. 15. pp. 658–660.

The authors note that, following on the work of CHAGAS on the development of *Schizotrypanum cruzi*, CARINI discovered cysts in the lungs of rats infected with *Trypanosoma lewisi*, which cysts he considered were schizogonic stages of the flagellate. These cysts measured, on an average, 5 μ in diameter, and were usually oval. They enclose eight vermicules, which appear to be binucleate.

At first agreeing with CARINI's interpretations, the authors however record that (1) rats immune to *T. lewisi* continue to show numerous cysts in their lungs; (2) inoculation of young rats with an emulsion, rich in cysts, derived from immune rats, was not followed by the appearance of trypanosomes in the blood-stream. Adult rats were more frequently parasitised than young rats. Of 22 adult rats the cysts of CARINI were found in all, but none was infected with *T. lewisi*.

The lung-cysts are transmissible by direct contagion. The authors conclude that the pneumocysts of CARINI represent a new parasite of rats. If the parasite is worthy of generic rank they propose for it the name *Pneumocystis carinii*. The affinities are, perhaps, to be sought among the Coccidia.

H. B. F.

BOOK REVIEW.

DANIELS (C. W.) and NEWHAM (H. B.). **Laboratory Studies in Tropical Medicine.** 3rd Edition. Demy 8vo. 535 pages. 164 text figures, 7 charts, and 6 coloured plates. 1911: London: John Bale, Sons & Danielsson, Ltd. (Price 16*s*. net.)

In the preface to the third edition of this well known text book the authors state that since the appearance of the last edition many advances have been made in the study of tropical diseases; new facts dealing with disease and its propagation have been made out and new details of technique have been elaborated. The book follows the tradition of the previous editions in being essentially practical. Brief descriptions of the more important protozoa, helminths, etc., are given, but in no sense is the book to be taken as a complete account of parasites in general. As the authors state, the classification of parasites and insects is constantly changing as new facts come to light; no authoritative schemes of classification are therefore given. Those inserted have been found by practice to be useful, and although differing in many details from those adopted by authorities at the moment, will, the authors believe, be of utility to the average man. New details have been added, which it is trusted will enhance the value of the book as an aid to the practical worker. The type is clear and there are many illustrations. More of these could have been incorporated with advantage. The contents follow the order of the practical course given at the London School of Tropical Medicine. A practical work such as the above must be in the hands of all workers in tropical medicine and those of the present time may congratulate themselves upon having the details of such an intricate subject presented to them in so compact and readable a form. The work is a popular one and deservedly so.

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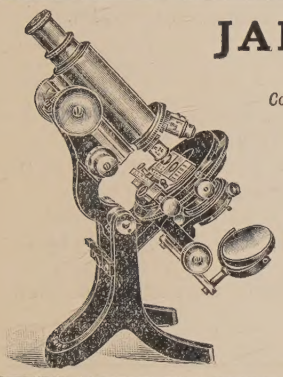

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